```
=> file medline
FILE 'MEDLINE' ENTERED AT 16:38:41 ON 28 APR 2006

 FILE LAST UPDATED: 27 APR 2006 (20060427/UP). FILE COVERS 1950 TO DATE.

 On December 11, 2005, the 2006 MeSH terms were loaded.

 The MEDLINE reload for 2006 is now (26 Feb.) available. For details
 on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
 See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

 OLDMEDLINE is covered back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2006 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que l27

L16        1164 SEA FILE=MEDLINE ABB=ON  PLU=ON  ("FUJII S"/AU OR "FUJII
                SEISHIRO"/AU)
L17          26 SEA FILE=MEDLINE ABB=ON  PLU=ON  ("DOTTO P"/AU OR "DOTTO
                PAOLO"/AU)
L18         200 SEA FILE=MEDLINE ABB=ON  PLU=ON  ("HAN R"/AU OR "HAN R C"/AU
                OR "HAN R F"/AU OR "HAN R J"/AU OR "HAN R K"/AU OR "HAN R
                L"/AU OR "HAN R N"/AU OR "HAN R O"/AU OR "HAN R S"/AU OR "HAN
                R X"/AU OR "HAN R Y"/AU OR "HAN R Z"/AU OR "HAN RONG"/AU OR
                "HAN RONG BIN"/AU)
L19          26 SEA FILE=MEDLINE ABB=ON  PLU=ON  ("BRISSETTE J"/AU OR "BRISSETT
                E J L"/AU OR "BRISSETTE JANICE L"/AU)
L20        2050 SEA FILE=MEDLINE ABB=ON  PLU=ON  RHO GTP-BINDING PROTEINS/CT
L21      171376 SEA FILE=MEDLINE ABB=ON  PLU=ON  SIGNAL TRANSDUCTION+NT/CT
L22        1597 SEA FILE=MEDLINE ABB=ON  PLU=ON  INTRACELLULAR SIGNALING
                PEPTIDES AND PROTEINS/CT
L23       27550 SEA FILE=MEDLINE ABB=ON  PLU=ON  (P21 OR P(2A)21 OR P21
                PROTEIN KINASE OR P21 SIGNAL TRANSDUCT?)
L24        2229 SEA FILE=MEDLINE ABB=ON  PLU=ON  SKIN AGING/CT
L26        2182 SEA FILE=MEDLINE ABB=ON  PLU=ON  (WRINKL? OR SKIN WRINKL? OR
                WRINK? REDUC?)
L27           0 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L16 OR L17 OR L18 OR L19)
                AND (L20 OR L21 OR L22 OR L23) AND (L24 OR L26)


=> s l27

L103          0 (L16 OR L17 OR L18 OR L19) AND (L20 OR L21 OR L22 OR L23) AND
                (L24 OR L26)

=> file wpix

FILE 'WPIX' ENTERED AT 16:38:44 ON 28 APR 2006
COPYRIGHT (C) 2006 THE THOMSON CORPORATION
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FILE LAST UPDATED:          26 APR 2006      <20060426/UP>
MOST RECENT DERWENT UPDATE:     200627        <200627/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/


>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<



>>>  UPCOMING NEW DWPI: EFFECTS ON SCRIPT RUNS - SEE NEWS MESSAGE <<<
'BIX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

=> d que l85

L77          766 SEA FILE=WPIX ABB=ON  PLU=ON  ("FUJII S"/AU OR "FUJII S I
                 C"/AU OR "FUJII S K"/AU OR "FUJII S N"/AU)
L78            3 SEA FILE=WPIX ABB=ON  PLU=ON  ("DOTTO G P"/AU OR "DOTTO P"/AU)

L79          118 SEA FILE=WPIX ABB=ON  PLU=ON  ("HAN R"/AU OR "HAN R A"/AU OR
                 "HAN R G"/AU OR "HAN R H"/AU OR "HAN R J L"/AU OR "HAN R L"/AU
                 OR "HAN R S"/AU OR "HAN R Y"/AU)
L80            6 SEA FILE=WPIX ABB=ON  PLU=ON  ("BRISSETTE J"/AU OR "BRISSETTE
                 J E"/AU OR "BRISSETTE J W"/AU)
L81           16 SEA FILE=WPIX ABB=ON  PLU=ON  P21/BIX (L) SIGNAL TRANSDUCT?/BIX

L82           39 SEA FILE=WPIX ABB=ON  PLU=ON  P21/BIX (L) PROTEIN KINAS?/BIX
L83          951 SEA FILE=WPIX ABB=ON  PLU=ON  (P21/BIX OR P 21/BIX)
L84        22202 SEA FILE=WPIX ABB=ON  PLU=ON  (WRINKL?/BIX OR SKIN WRINKL?/BIX
                 OR WRINK? REDUC?/BIX OR SKIN AGING/BIX OR SKIN AGEING/BIX OR
                 PHOTO/BIX (L) (AGING/BIX OR AGEING/BIX))
L85            1 SEA FILE=WPIX ABB=ON  PLU=ON  (L77 OR L78 OR L79 OR L80) AND
                 (L81 OR L82 OR L83) AND L84


=> s l85

L104           1 (L77 OR L78 OR L79 OR L80) AND (L81 OR L82 OR L83) AND L84

=> file biosis

FILE 'BIOSIS' ENTERED AT 16:38:48 ON 28 APR 2006
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 26 April 2006 (20060426/ED)


=> d que l74
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L65          225 SEA FILE=BIOSIS ABB=ON  PLU=ON  P21 PROTEIN/CT
L66         3066 SEA FILE=BIOSIS ABB=ON  PLU=ON  P21/CT
L67            4 SEA FILE=BIOSIS ABB=ON  PLU=ON  SKIN AGING/CT
L68         2118 SEA FILE=BIOSIS ABB=ON  PLU=ON  (SKIN OR PHOTO) (L) (AGING OR
                 AGEING)
L69         2403 SEA FILE=BIOSIS ABB=ON  PLU=ON  (WRINKL? OR SKIN WRINKL? OR
                 WRINK? REDUC?)
L70         1038 SEA FILE=BIOSIS ABB=ON  PLU=ON  ("FUJII S"/AU OR "FUJII S
                 F"/AU OR "FUJII S I"/AU OR "FUJII S Y KURODA"/AU OR "FUJII
                 SEISHIRO"/AU)
L71           68 SEA FILE=BIOSIS ABB=ON  PLU=ON  ("DOTTO P"/AU OR "DOTTO P
                 A"/AU OR "DOTTO P G"/AU OR "DOTTO PAOLA"/AU OR "DOTTO PAOLO"/AU
                  OR "DOTTO PAOLO D"/AU OR "DOTTO PAOLO G"/AU)
L72          141 SEA FILE=BIOSIS ABB=ON  PLU=ON  ("HAN R"/AU OR "HAN R C"/AU OR
                 "HAN R F"/AU OR "HAN R I"/AU OR "HAN R J"/AU OR "HAN R J L"/AU
                 OR "HAN R K"/AU OR "HAN R K W"/AU OR "HAN R M"/AU OR "HAN R
                 N"/AU OR "HAN R N N"/AU OR "HAN R O"/AU OR "HAN R W"/AU OR
                 "HAN R Y"/AU OR "HAN R Z"/AU OR "HAN RONG"/AU OR "HAN RONG
                 LAN"/AU OR "HAN RONG RONG"/AU OR "HAN RONG ZHUANG"/AU)
L73           57 SEA FILE=BIOSIS ABB=ON  PLU=ON  ("BRISSETTE J"/AU OR "BRISSETTE
                  J C"/AU OR "BRISSETTE J L"/AU OR "BRISSETTE JANICE"/AU OR
                 "BRISSETTE JANICE L"/AU)
L74            0 SEA FILE=BIOSIS ABB=ON  PLU=ON  (L70 OR L71 OR L72 OR L73) AND
                 (L65 OR L66) AND (L67 OR L68 OR L69)


=> s l74

L105           0 (L70 OR L71 OR L72 OR L73) AND (L65 OR L66) AND (L67 OR L68 OR
                 L69)

=> file caplus

FILE 'CAPLUS' ENTERED AT 16:38:50 ON 28 APR 2006
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FILE COVERS 1907 - 28 Apr 2006  VOL 144 ISS 19
FILE LAST UPDATED: 27 Apr 2006  (20060427/ED)

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They are available for your review at:

http://www.cas.org/infopolicy.html

=> d que l15; d que l61
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L1          658 SEA FILE=CAPLUS ABB=ON  PLU=ON  P21-ACTIVATED KINASE/CT
L2            0 SEA FILE=CAPLUS ABB=ON  PLU=ON  PROTEINS (L) P21/CT
L3            0 SEA FILE=CAPLUS ABB=ON  PLU=ON  PROTEINS (L) SIGNALING+OLD/CT
L4       142893 SEA FILE=CAPLUS ABB=ON  PLU=ON  SIGNAL TRANSDUCTION/CT
L5        88152 SEA FILE=CAPLUS ABB=ON  PLU=ON  (P21 OR P(2A)21 OR P21 PROTEIN
                KINASE OR P21 SIGNAL TRANSDUCTION? OR P21?)
L7        11170 SEA FILE=CAPLUS ABB=ON  PLU=ON  (WRINKL? OR SKIN WRINKL? OR
                WRINK? REDUC?)
L8           25 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4 OR L5)
                AND L7
L11         356 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("FUJII S"/AU OR "FUJII
                SEISHIRO"/AU)
L12          13 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("DOTTO P"/AU OR "DOTTO P
                DEL"/AU OR "DOTTO PAOLA"/AU OR "DOTTO PAOLO"/AU OR "DOTTO
                PAOLO DEL"/AU)
L13         154 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("HAN R"/AU OR "HAN R D"/AU OR
                "HAN R F"/AU OR "HAN R J"/AU OR "HAN R K W"/AU OR "HAN R M"/AU
                OR "HAN R N N"/AU OR "HAN R P"/AU OR "HAN R Q"/AU OR "HAN R
                S"/AU OR "HAN R T"/AU OR "HAN R X"/AU OR "HAN R Y"/AU OR "HAN
                RONG"/AU OR "HAN RONG BI"/AU OR "HAN RONG BIN"/AU OR "HAN RONG
                DI"/AU OR "HAN RONG DIAN"/AU OR "HAN RONG JIANG"/AU OR "HAN
                RONG RONG"/AU)
L14          29 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("BRISSETTE J"/AU OR "BRISSETTE
                 JANICE"/AU OR "BRISSETTE JANICE L"/AU OR "BRISSETTE JANICE
                LYNN"/AU)
L15           1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND (L11 OR L12 OR L13 OR
                L14)



L11         356 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("FUJII S"/AU OR "FUJII
                SEISHIRO"/AU)
L12          13 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("DOTTO P"/AU OR "DOTTO P
                DEL"/AU OR "DOTTO PAOLA"/AU OR "DOTTO PAOLO"/AU OR "DOTTO
                PAOLO DEL"/AU)
L13         154 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("HAN R"/AU OR "HAN R D"/AU OR
                "HAN R F"/AU OR "HAN R J"/AU OR "HAN R K W"/AU OR "HAN R M"/AU
                OR "HAN R N N"/AU OR "HAN R P"/AU OR "HAN R Q"/AU OR "HAN R
                S"/AU OR "HAN R T"/AU OR "HAN R X"/AU OR "HAN R Y"/AU OR "HAN
                RONG"/AU OR "HAN RONG BI"/AU OR "HAN RONG BIN"/AU OR "HAN RONG
                DI"/AU OR "HAN RONG DIAN"/AU OR "HAN RONG JIANG"/AU OR "HAN
                RONG RONG"/AU)
L14          29 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("BRISSETTE J"/AU OR "BRISSETTE
                 JANICE"/AU OR "BRISSETTE JANICE L"/AU OR "BRISSETTE JANICE
                LYNN"/AU)
L56           8 SEA FILE=CAPLUS ABB=ON  PLU=ON  SKIN, DISEASE (L) AGING+OLD/CT

L57           0 SEA FILE=CAPLUS ABB=ON  PLU=ON  PHOTO AGING/CT
L58        5521 SEA FILE=CAPLUS ABB=ON  PLU=ON  (SKIN OR PHOTO) (L) (AGING OR
                AGEING)
L61           6 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L56 OR L57 OR L58) AND (L11
                OR L12 OR L13 OR L14)


=> s l15,l61

L106          6 (L15 OR L61)

=> file embase
```

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FILE 'EMBASE' ENTERED AT 16:38:53 ON 28 APR 2006
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 FILE COVERS 1974 TO 28 Apr 2006 (20060428/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 EMBASE is now updated daily.  SDI frequency remains weekly (default)
 and biweekly.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que l47

L39          106 SEA FILE=EMBASE ABB=ON  PLU=ON  P21 ACTIVATED KINASE?/CT
L40         1517 SEA FILE=EMBASE ABB=ON  PLU=ON  P21 (L) (PROTEIN KINAS? OR
                 SIGNAL TRANSDUCT?)
L41          477 SEA FILE=EMBASE ABB=ON  PLU=ON  WRINKLE/CT
L42         2415 SEA FILE=EMBASE ABB=ON  PLU=ON  (WRINKL? OR SKIN WRINKL? OR
                 WRINK? REDUC?)
L43         1239 SEA FILE=EMBASE ABB=ON  PLU=ON  ("FUJII S"/AU OR "FUJII S
                 I"/AU OR "FUJII S K"/AU OR "FUJII S Y"/AU)
L44           45 SEA FILE=EMBASE ABB=ON  PLU=ON  ("DOTTO P"/AU OR "DOTTO P D
                 F"/AU)
L45          206 SEA FILE=EMBASE ABB=ON  PLU=ON  ("HAN R"/AU OR "HAN R C"/AU OR
                 "HAN R F"/AU OR "HAN R G"/AU OR "HAN R J"/AU OR "HAN R J L"/AU
                 OR "HAN R K"/AU OR "HAN R L"/AU OR "HAN R N"/AU OR "HAN R N
                 N"/AU OR "HAN R O"/AU OR "HAN R S"/AU OR "HAN R T"/AU OR "HAN
                 R W"/AU OR "HAN R Y"/AU OR "HAN R Y H"/AU OR "HAN R Z"/AU OR
                 "HAN RONG QIN"/AU)
L46           25 SEA FILE=EMBASE ABB=ON  PLU=ON  ("BRISSETTE J"/AU OR "BRISSETTE
                  J L"/AU)
L47            0 SEA FILE=EMBASE ABB=ON  PLU=ON  (L43 OR L44 OR L45 OR L46) AND
                 (L39 OR L40) AND (L41 OR L42)


=> s l47

L107           0 (L43 OR L44 OR L45 OR L46) AND (L39 OR L40) AND (L41 OR L42)

=> file home

FILE 'HOME' ENTERED AT 16:38:55 ON 28 APR 2006

=> => dup rem l103-l107
L103 HAS NO ANSWERS
L105 HAS NO ANSWERS
L107 HAS NO ANSWERS
FILE 'WPIX' ENTERED AT 16:40:56 ON 28 APR 2006
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PROCESSING COMPLETED FOR L103
PROCESSING COMPLETED FOR L104
PROCESSING COMPLETED FOR L105
PROCESSING COMPLETED FOR L106
```

PROCESSING COMPLETED FOR L107
L108 6 DUP REM L103-L107 (1 DUPLICATE REMOVED)
ANSWER '1' FROM FILE WPIX
ANSWERS '2-6' FROM FILE CAPLUS

=> d all abs abeq tech 1;d ibib ed abs hitind 2-6

L108 ANSWER 1 OF 6 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN DUPLICATE 1
AN 2004-295301 [27] WPIX
DNC C2004-112970
TI Screening of **wrinkle-reducing** agents useful for treating **wrinkles** involves determination of the test agent and correlating the ability of the test agent.
DC B04 D16 D21
IN **BRISSETTE, J**; **DOTTO, P**; **FUJII, S**; **HAN, R**
PA (BRIS-I) BRISSETTE J; (DOTT-I) DOTTO P; (FUJI-I) FUJII S; (HANR-I) HAN R; (GEHO) GEN HOSPITAL CORP
CYC 3
PI WO 2004026249 A2 20040401 (200427)* EN 20 A61K000-00
W: CA JP
US 2004110203 A1 20040610 (200438) C12Q001-00
JP 2006504932 W 20060209 (200612) 14 G01N033-50
ADT WO 2004026249 A2 WO 2003-US29496 20030919; US 2004110203 A1 Provisional US 2002-412503P 20020920, US 2003-664795 20030919; JP 2006504932 W WO 2003-US29496 20030919, JP 2004-538235 20030919
FDT JP 2006504932 W Based on WO 2004026249
PRAI US 2002-412503P 20020920; US 2003-664795 20030919
IC ICM A61K000-00; C12Q001-00; G01N033-50
ICS A61K008-00; A61Q017-00; C12Q001-68; G01N033-15
AB WO2004026249 A UPAB: 20040426
NOVELTY - Screening of **wrinkles reducing** agent involves determination of the test agent to increase or induces a component (C1) of the **p21 signal transduction** pathway and correlating the ability of the test agent to increase expression, activity or levels of (C1) with the agent's ability to reduce the appearance or formation of **wrinkles.**
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(a) a cosmetic composition comprising an agent that increases or induces **p21**;
(b) providing a record involves determination of the test agent to increase or induces **p21**;
(c) generating the record that correlates the ability of the test agent; and
(d) a kit comprises a composition comprising an agent that increases or induces (C1); and instructions for using the composition.
ACTIVITY - Dermatological.
MECHANISM OF ACTION - None given.
USE - As a cosmetic for preventing or treating **wrinkles**, for reducing the appearance or formation of **wrinkles** on the skin (claimed) and in the manufacture of medicament for preventing skin damage e.g. UVB-induce skin damage.
ADVANTAGE - The **p21 signal transduction** pathway prevents skin damage, reduces the appearance or formation of **wrinkles** on the skin and UVB-induce skin damage.
Dwg.0/0
FS CPI
FA AB
MC CPI: B04-E02F; B04-E05; B04-F0200E; B04-N0200E; B11-C08E1; B11-C08F2; B11-C08F4; B11-C10; B12-K04E; B12-K04F; B14-N17C; B14-R05; D05-H08;

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     AT 16:51:47 ON 28 APR 2006
                 D QUE L97
L114              1 SEA ABB=ON  PLU=ON  L97

     FILE 'HOME' ENTERED AT 16:51:52 ON 28 APR 2006

     FILE 'STNGUIDE' ENTERED AT 16:52:02 ON 28 APR 2006

     FILE 'MEDLINE, WPIX, BIOSIS, CAPLUS, USPATFULL, BIOTECHNO' ENTERED AT
     16:52:54 ON 28 APR 2006
L115             13 DUP REM L109-L114 (0 DUPLICATES REMOVED)
                        ANSWERS '1-5' FROM FILE MEDLINE
                        ANSWER '6' FROM FILE WPIX
                        ANSWERS '7-10' FROM FILE BIOSIS
                        ANSWER '11' FROM FILE CAPLUS
                        ANSWER '12' FROM FILE USPATFULL
                        ANSWER '13' FROM FILE BIOTECHNO
                   D IALL 1-5
                   D ALL ABS ABEQ TECH 6
                   D IALL 7-10
                   D IBIB ED ABS HITIND 11
                   D IALL 13

     FILE 'USPATFULL' ENTERED AT 17:00:19 ON 28 APR 2006

     FILE 'STNGUIDE' ENTERED AT 17:02:08 ON 28 APR 2006

     FILE 'USPATFULL' ENTERED AT 17:04:31 ON 28 APR 2006

     FILE 'USPATFULL' ENTERED AT 17:04:46 ON 28 APR 2006
                 D IBIB ABS HIT L100 TOT

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                OR L22 OR L23) AND (L24 OR L26)

     FILE 'WPIX' ENTERED AT 16:38:44 ON 28 APR 2006
                D QUE L85
L104          1 SEA ABB=ON  PLU=ON  (L77 OR L78 OR L79 OR L80) AND (L81 OR L82
                OR L83) AND L84

     FILE 'BIOSIS' ENTERED AT 16:38:48 ON 28 APR 2006
                D QUE L74
L105          0 SEA ABB=ON  PLU=ON  (L70 OR L71 OR L72 OR L73) AND (L65 OR
                L66) AND (L67 OR L68 OR L69)

     FILE 'CAPLUS' ENTERED AT 16:38:50 ON 28 APR 2006
                D QUE L15
                D QUE L61
L106          6 SEA ABB=ON  PLU=ON  (L15 OR L61)

     FILE 'EMBASE' ENTERED AT 16:38:53 ON 28 APR 2006
                D QUE L47
L107          0 SEA ABB=ON  PLU=ON  (L43 OR L44 OR L45 OR L46) AND (L39 OR
                L40) AND (L41 OR L42)

     FILE 'HOME' ENTERED AT 16:38:55 ON 28 APR 2006

     FILE 'STNGUIDE' ENTERED AT 16:39:02 ON 28 APR 2006

     FILE 'WPIX, CAPLUS' ENTERED AT 16:40:56 ON 28 APR 2006
L108          6 DUP REM L103-L107 (1 DUPLICATE REMOVED)
                     ANSWER '1' FROM FILE WPIX
                     ANSWERS '2-6' FROM FILE CAPLUS
                D ALL ABS ABEQ TECH 1
                D IBIB ED ABS HITIND 2-6

     FILE 'MEDLINE' ENTERED AT 16:51:32 ON 28 APR 2006
                D QUE L55
L109          5 SEA ABB=ON  PLU=ON  L55 NOT L27

     FILE 'WPIX' ENTERED AT 16:51:35 ON 28 APR 2006
                D QUE L86
L110          1 SEA ABB=ON  PLU=ON  L86 NOT L85

     FILE 'BIOSIS' ENTERED AT 16:51:38 ON 28 APR 2006
                D QUE L76
L111          4 SEA ABB=ON  PLU=ON  L76 NOT L74

     FILE 'CAPLUS' ENTERED AT 16:51:41 ON 28 APR 2006
                D QUE L38
                D QUE L60
                D QUE L88
                D QUE L90
                D QUE L101
                D QUE L102
L112          1 SEA ABB=ON  PLU=ON  (L38 OR L60 OR L88 OR L90 OR L101 OR L102)
                NOT (L15 OR L61)

     FILE 'USPATFULL' ENTERED AT 16:51:44 ON 28 APR 2006
                D QUE L100
L113          1 SEA ABB=ON  PLU=ON  L99 AND L98

     FILE 'PASCAL, BIOTECHNO, ESBIOBASE, TOXCENTER, KOSMET, SCISEARCH' ENTERED
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                1   FILE FRFULL
                2   FILE GBFULL
                4   FILE IFIPAT
                2   FILE INPADOC
                3   FILE KOSMET
                6   FILE MEDLINE
                3   FILE NLDB
                1   FILE NUTRACEUT
                4   FILE PASCAL
                1   FILE PATDPAFULL
               73   FILE PCTFULL
                6   FILE PHIN
                7   FILE PROMT
                7   FILE SCISEARCH
                6   FILE TOXCENTER
              178   FILE USPATFULL
               26   FILE USPAT2
                3   FILE WPIDS
                3   FILE WPINDEX
L91              QUE ABB=ON  PLU=ON  (P21 OR P 21) AND (WRINKL? OR PHOTOAG? OR
                 SKIN (2A)(AGING OR AGEING))
                 ---------
                 D RANK

     FILE 'PASCAL, BIOTECHNO, ESBIOBASE, TOXCENTER, KOSMET, SCISEARCH' ENTERED
     AT 16:19:35 ON 28 APR 2006
L92         45765 SEA ABB=ON  PLU=ON  (P21 OR P 21)
L93         14267 SEA ABB=ON  PLU=ON  (WRINKL? OR PHOTOAG? OR SKIN (2A)(AGING OR
                  AGEING))
L94            30 SEA ABB=ON  PLU=ON  L92 AND L93
L95            11 DUP REM L94 (19 DUPLICATES REMOVED)
                       ANSWERS '1-4' FROM FILE PASCAL
                       ANSWERS '5-6' FROM FILE BIOTECHNO
                       ANSWER '7' FROM FILE ESBIOBASE
                       ANSWER '8' FROM FILE TOXCENTER
                       ANSWERS '9-11' FROM FILE KOSMET
                 D SCAN
L96             1 SEA ABB=ON  PLU=ON  L95 AND DRUG EFFECTS/CT
                 D SCAN
L97             1 SEA ABB=ON  PLU=ON  L95 AND DRUG EFFECT/CT
                 D SCAN

     FILE 'USPATFULL' ENTERED AT 16:23:38 ON 28 APR 2006
L98           612 SEA ABB=ON  PLU=ON  (P21 OR P 21)/TI,IT,AB,CLM
L99          5951 SEA ABB=ON  PLU=ON  (WRINKL? OR PHOTOAG? OR SKIN (2A)(AGING OR
                  AGEING))/TI,IT,AB,CLM
L100            1 SEA ABB=ON  PLU=ON  L99 AND L98
                 D SCAN
                 D KWIC

     FILE 'CAPLUS' ENTERED AT 16:27:52 ON 28 APR 2006
L101            2 SEA ABB=ON  PLU=ON  L8 AND (P21 OR P 21)
                 D SCAN
                 D TI L61 1-6
L102            1 SEA ABB=ON  PLU=ON  L61 AND (P21 OR P 21)
                 D SCAN

     FILE 'MEDLINE' ENTERED AT 16:38:41 ON 28 APR 2006
                 D QUE L27
L103            0 SEA ABB=ON  PLU=ON  (L16 OR L17 OR L18 OR L19) AND (L20 OR L21
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                E SIGNAL TRANSDUCTION/CT
                E PROTEIN/CT
L83          951 SEA ABB=ON  PLU=ON  (P21/BIX OR P 21/BIX)
                E WRINKLES/CT
                E WRINKLE/CT
                E SKIN AGING/CT
L84        22202 SEA ABB=ON  PLU=ON  (WRINKL?/BIX OR SKIN WRINKL?/BIX OR WRINK?
                REDUC?/BIX OR SKIN AGING/BIX OR SKIN AGEING/BIX OR PHOTO/BIX
                (L) (AGING/BIX OR AGEING/BIX))
L85            1 SEA ABB=ON  PLU=ON  (L77 OR L78 OR L79 OR L80) AND (L81 OR L82
                OR L83) AND L84
                D SCAN
L86            2 SEA ABB=ON  PLU=ON  (L81 OR L82 OR L83) AND L84
                D SCAN
                D BROWSE L85

     FILE 'STNGUIDE' ENTERED AT 15:31:34 ON 28 APR 2006

     FILE 'WPIX' ENTERED AT 15:44:39 ON 28 APR 2006
                E A61K000/IPC
                E A61K000-00C
                E A61K000-00/IPC
                E A61K000-00/ICM,ICS,ICA
L*** DEL     464 S E4
                D HIT

     FILE 'STNGUIDE' ENTERED AT 15:46:56 ON 28 APR 2006

     FILE 'WPIX' ENTERED AT 15:55:13 ON 28 APR 2006
                E AK1K008-00/ICM,ICS,ICA

     FILE 'STNGUIDE' ENTERED AT 15:57:44 ON 28 APR 2006

     FILE 'WPIX' ENTERED AT 16:00:21 ON 28 APR 2006

     FILE 'CAPLUS' ENTERED AT 16:05:03 ON 28 APR 2006
                D QUE L8
                E SCREENING/CT
                E E4+ALL
                E E2+ALL
L87        46461 SEA ABB=ON  PLU=ON  SCREENING/CW
L88            0 SEA ABB=ON  PLU=ON  L87 AND L8
                D SCAN TI L8
                D QUE L8
L89       734780 SEA ABB=ON  PLU=ON  9/SC,SX
L90            0 SEA ABB=ON  PLU=ON  L8 AND L89

     INDEX '1MOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE, AGRICOLA,
     ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE, BABS,
     BIBLIODATA, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA,
     CAOLD, CAPLUS, CASREACT, CBNB, CEABA-VTB, CERAB, ...' ENTERED AT 16:12:22
     ON 28 APR 2006
                SEA (P21 OR P 21) AND (WRINKL? OR PHOTOAG? OR SKIN (2A)(AGING O
               ---------
                5   FILE BIOSIS
                4   FILE BIOTECHNO
                7   FILE CAPLUS
                7   FILE EMBASE
               25   FILE EPFULL
                6   FILE ESBIOBASE
```

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L64           0 SEA ABB=ON  PLU=ON  (L62 OR L49) AND (L43 OR L44 OR L45 OR
                L46)

     FILE 'BIOSIS' ENTERED AT 14:09:20 ON 28 APR 2006
                E P21/CT
L65         225 SEA ABB=ON  PLU=ON  P21 PROTEIN/CT
L66        3066 SEA ABB=ON  PLU=ON  P21/CT
                E SKIN AGING/CT
L67           4 SEA ABB=ON  PLU=ON  SKIN AGING/CT
                E PHOTO AGING/CT
L68        2118 SEA ABB=ON  PLU=ON  (SKIN OR PHOTO) (L) (AGING OR AGEING)
                E WRINKLE/CT
L69        2403 SEA ABB=ON  PLU=ON  (WRINKL? OR SKIN WRINKL? OR WRINK? REDUC?)


     FILE 'STNGUIDE' ENTERED AT 14:14:48 ON 28 APR 2006

     FILE 'BIOSIS' ENTERED AT 15:00:15 ON 28 APR 2006
                E FUJII S/AU
L70        1038 SEA ABB=ON  PLU=ON  ("FUJII S"/AU OR "FUJII S F"/AU OR "FUJII
                S I"/AU OR "FUJII S Y KURODA"/AU OR "FUJII SEISHIRO"/AU)
                E DOTTO P/AU
L71          68 SEA ABB=ON  PLU=ON  ("DOTTO P"/AU OR "DOTTO P A"/AU OR "DOTTO
                P G"/AU OR "DOTTO PAOLA"/AU OR "DOTTO PAOLO"/AU OR "DOTTO
                PAOLO D"/AU OR "DOTTO PAOLO G"/AU)
                E HAN R/AU
L72         141 SEA ABB=ON  PLU=ON  ("HAN R"/AU OR "HAN R C"/AU OR "HAN R
                F"/AU OR "HAN R I"/AU OR "HAN R J"/AU OR "HAN R J L"/AU OR
                "HAN R K"/AU OR "HAN R K W"/AU OR "HAN R M"/AU OR "HAN R N"/AU
                OR "HAN R N N"/AU OR "HAN R O"/AU OR "HAN R W"/AU OR "HAN R
                Y"/AU OR "HAN R Z"/AU OR "HAN RONG"/AU OR "HAN RONG LAN"/AU OR
                "HAN RONG RONG"/AU OR "HAN RONG ZHUANG"/AU)
                E BRISSETTE J/AU
L73          57 SEA ABB=ON  PLU=ON  ("BRISSETTE J"/AU OR "BRISSETTE J C"/AU OR
                "BRISSETTE J L"/AU OR "BRISSETTE JANICE"/AU OR "BRISSETTE
                JANICE L"/AU)
L74           0 SEA ABB=ON  PLU=ON  (L70 OR L71 OR L72 OR L73) AND (L65 OR
                L66) AND (L67 OR L68 OR L69)
L75           4 SEA ABB=ON  PLU=ON  (L65 OR L66) AND (L67 OR L68 OR L69)
                D SCAN
L76           4 SEA ABB=ON  PLU=ON  L75 AND (P21 OR P 21)
                D KWIC

     FILE 'WPIX' ENTERED AT 15:11:11 ON 28 APR 2006
                E FUJII S/AU
L77         766 SEA ABB=ON  PLU=ON  ("FUJII S"/AU OR "FUJII S I C"/AU OR
                "FUJII S K"/AU OR "FUJII S N"/AU)
                E DOTTO P/AU
                E DOTTO/AU
L78           3 SEA ABB=ON  PLU=ON  ("DOTTO G P"/AU OR "DOTTO P"/AU)
                E HAN R/AU
L79         118 SEA ABB=ON  PLU=ON  ("HAN R"/AU OR "HAN R A"/AU OR "HAN R
                G"/AU OR "HAN R H"/AU OR "HAN R J L"/AU OR "HAN R L"/AU OR
                "HAN R S"/AU OR "HAN R Y"/AU)
                E BRISSETTE J/AU
L80           6 SEA ABB=ON  PLU=ON  ("BRISSETTE J"/AU OR "BRISSETTE J E"/AU OR
                "BRISSETTE J W"/AU)
                E P21/CT
L81          16 SEA ABB=ON  PLU=ON  P21/BIX (L) SIGNAL TRANSDUCT?/BIX
L82          39 SEA ABB=ON  PLU=ON  P21/BIX (L) PROTEIN KINAS?/BIX
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L43        1239 SEA ABB=ON  PLU=ON  ("FUJII S"/AU OR "FUJII S I"/AU OR "FUJII
                S K"/AU OR "FUJII S Y"/AU)
                E DOTTO P/AU
L44          45 SEA ABB=ON  PLU=ON  ("DOTTO P"/AU OR "DOTTO P D F"/AU)
                E HAN R/AU
L45         206 SEA ABB=ON  PLU=ON  ("HAN R"/AU OR "HAN R C"/AU OR "HAN R
                F"/AU OR "HAN R G"/AU OR "HAN R J"/AU OR "HAN R J L"/AU OR
                "HAN R K"/AU OR "HAN R L"/AU OR "HAN R N"/AU OR "HAN R N N"/AU
                OR "HAN R O"/AU OR "HAN R S"/AU OR "HAN R T"/AU OR "HAN R
                W"/AU OR "HAN R Y"/AU OR "HAN R Y H"/AU OR "HAN R Z"/AU OR
                "HAN RONG QIN"/AU)
                E BRISSETTE J/AU
L46          25 SEA ABB=ON  PLU=ON  ("BRISSETTE J"/AU OR "BRISSETTE J L"/AU)
L47           0 SEA ABB=ON  PLU=ON  (L43 OR L44 OR L45 OR L46) AND (L39 OR
                L40) AND (L41 OR L42)
L48           0 SEA ABB=ON  PLU=ON  (L39 OR L40) AND (L41 OR L42)
L49        2464 SEA ABB=ON  PLU=ON  (SKIN OR PHOTO) (L) (AGING OR AGEING)
L50           0 SEA ABB=ON  PLU=ON  L49 AND (L39 OR L40)

     FILE 'MEDLINE' ENTERED AT 13:58:06 ON 28 APR 2006
                E SKIN AGING/CT
                E E3+ALL
L51        2229 SEA ABB=ON  PLU=ON  SKIN AGING/CT
                E PHOTO AGING/CT
L52        4153 SEA ABB=ON  PLU=ON  (SKIN OR PHOTO) (L) (AGING OR AGEING)
L53          64 SEA ABB=ON  PLU=ON  (L51 OR L52) AND (L20 OR L21 OR L22 OR
                L23)
L54          12 SEA ABB=ON  PLU=ON  L53 AND (P21 OR P 21)
                D TRIAL
                D KWIC
                D KWIC 2
                D TI 1-12
L55           5 SEA ABB=ON  PLU=ON  L54 NOT PY>2002
                D KWIC

     FILE 'CAPLUS' ENTERED AT 14:01:58 ON 28 APR 2006
                E SKIN AGING/CT
                E E3+ALL
                E E2+ALL
L56           8 SEA ABB=ON  PLU=ON  SKIN, DISEASE (L) AGING+OLD/CT
                E PHOTO AGING/CT
L57           0 SEA ABB=ON  PLU=ON  PHOTO AGING/CT
L58        5521 SEA ABB=ON  PLU=ON  (SKIN OR PHOTO) (L) (AGING OR AGEING)
L59         979 SEA ABB=ON  PLU=ON  (L56 OR L57 OR L58) AND L7
L60           1 SEA ABB=ON  PLU=ON  L59 AND (P21 OR P 21)
                D SCAN
L61           6 SEA ABB=ON  PLU=ON  (L56 OR L57 OR L58) AND (L11 OR L12 OR L13
                OR L14)
                D KWIC
                D TI 1-6
                D BIB

     FILE 'MEDLINE' ENTERED AT 14:05:56 ON 28 APR 2006

     FILE 'EMBASE' ENTERED AT 14:07:36 ON 28 APR 2006
                E SKIN AGING/CT
                E E3+ALL
                E E2+ALL
L62         669 SEA ABB=ON  PLU=ON  CUTANEOUS PARAMETERS/CT
L63           0 SEA ABB=ON  PLU=ON  (L62 OR L49) AND (L39 OR L40)
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                E WRINKLE/CT
                E E5+ALL
                E E2+ALL
L24         2229 SEA ABB=ON  PLU=ON  SKIN AGING/CT
                E WRINKLE/CT
                E SKIN WRINK/CT
                E E4+ALL
                E SKIN WRINK/CT
                E E5+ALL
                E PHOTOAGING/CT
                E E4+ALL
L25            0 SEA ABB=ON  PLU=ON  (L16 OR L17 OR L18 OR L19) AND (L20 OR L21
                  OR L22 OR L23) AND L24
L26         2182 SEA ABB=ON  PLU=ON  (WRINKL? OR SKIN WRINKL? OR WRINK? REDUC?)

L27            0 SEA ABB=ON  PLU=ON  (L16 OR L17 OR L18 OR L19) AND (L20 OR L21
                  OR L22 OR L23) AND (L24 OR L26)
L28           51 SEA ABB=ON  PLU=ON  (L20 OR L21 OR L22 OR L23) AND (L24 OR
                  L26)
L29           30 SEA ABB=ON  PLU=ON  L28 NOT PY>2002
L30            0 SEA ABB=ON  PLU=ON  L29 AND (P21 OR P 21)
                  D TRIAL L29
L31            0 SEA ABB=ON  PLU=ON  L30 AND L23
L32          371 SEA ABB=ON  PLU=ON  P21 (L) SIGNAL TRANSDUCT?
L33            0 SEA ABB=ON  PLU=ON  L32 AND L28
L34          924 SEA ABB=ON  PLU=ON  P21 (L) PROTEIN KINAS?
L35            0 SEA ABB=ON  PLU=ON  L34 AND L28
L36            0 SEA ABB=ON  PLU=ON  (L32 OR L34) AND (L16 OR L17 OR L18 OR
                  L19)

     FILE 'EMBASE' ENTERED AT 13:43:04 ON 28 APR 2006

     FILE 'CAPLUS' ENTERED AT 13:43:15 ON 28 APR 2006
L37         1259 SEA ABB=ON  PLU=ON  P21 (L) (PROTEIN KINAS? OR SIGNAL TRANSDUCT
                  ?)
L38            1 SEA ABB=ON  PLU=ON  L37 AND L7
                  D SCAN
                  D BIB

     FILE 'EMBASE' ENTERED AT 13:45:01 ON 28 APR 2006
                E P21/CT
L39          106 SEA ABB=ON  PLU=ON  P21 ACTIVATED KINASE?/CT
L40         1517 SEA ABB=ON  PLU=ON  P21 (L) (PROTEIN KINAS? OR SIGNAL TRANSDUCT
                  ?)
                E SIGNAL TRANSDUCT/CT
                E E4+ALL
                E SIGNAL TRANSDUCT/CT
                E WRINKLE/CT
                E E3+ALL
L41          477 SEA ABB=ON  PLU=ON  WRINKLE/CT
                E WRINKLE/CT
                E E12+ALL
                E SKIN AGING/CT
                E E3+ALL
                E E2+ALL
                E SKIN WRINKL/CT
                E E4+ALL
L42         2415 SEA ABB=ON  PLU=ON  (WRINKL? OR SKIN WRINKL? OR WRINK? REDUC?)

                E FUJII S/AU
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     FILE 'CAPLUS' ENTERED AT 13:10:13 ON 28 APR 2006
L10          14 SEA ABB=ON  PLU=ON  L8 NOT (PY>2002 OR AY>2002 OR PRY>2002)
                D TI 1-14
                E PHOTOAGIN/CT
                E E5+ALL
                E FUJII S/AU
L11         356 SEA ABB=ON  PLU=ON  ("FUJII S"/AU OR "FUJII SEISHIRO"/AU)
                E DOTTO P/AU
L12          13 SEA ABB=ON  PLU=ON  ("DOTTO P"/AU OR "DOTTO P DEL"/AU OR
                "DOTTO PAOLA"/AU OR "DOTTO PAOLO"/AU OR "DOTTO PAOLO DEL"/AU)
                E HAN R/AU
L13         154 SEA ABB=ON  PLU=ON  ("HAN R"/AU OR "HAN R D"/AU OR "HAN R
                F"/AU OR "HAN R J"/AU OR "HAN R K W"/AU OR "HAN R M"/AU OR
                "HAN R N N"/AU OR "HAN R P"/AU OR "HAN R Q"/AU OR "HAN R S"/AU
                OR "HAN R T"/AU OR "HAN R X"/AU OR "HAN R Y"/AU OR "HAN
                RONG"/AU OR "HAN RONG BI"/AU OR "HAN RONG BIN"/AU OR "HAN RONG
                DI"/AU OR "HAN RONG DIAN"/AU OR "HAN RONG JIANG"/AU OR "HAN
                RONG RONG"/AU)
                E BRISSETTE J/AU
L14          29 SEA ABB=ON  PLU=ON  ("BRISSETTE J"/AU OR "BRISSETTE JANICE"/AU
                OR "BRISSETTE JANICE L"/AU OR "BRISSETTE JANICE LYNN"/AU)
L15           1 SEA ABB=ON  PLU=ON  L8 AND (L11 OR L12 OR L13 OR L14)
                D SCAN L10

     FILE 'MEDLINE' ENTERED AT 13:25:44 ON 28 APR 2006
                E FUJII S/AU
L16        1164 SEA ABB=ON  PLU=ON  ("FUJII S"/AU OR "FUJII SEISHIRO"/AU)
                E DOTTO P/AU
L17          26 SEA ABB=ON  PLU=ON  ("DOTTO P"/AU OR "DOTTO PAOLO"/AU)
                E HAN R/AU
L18         200 SEA ABB=ON  PLU=ON  ("HAN R"/AU OR "HAN R C"/AU OR "HAN R
                F"/AU OR "HAN R J"/AU OR "HAN R K"/AU OR "HAN R L"/AU OR "HAN
                R N"/AU OR "HAN R O"/AU OR "HAN R S"/AU OR "HAN R X"/AU OR
                "HAN R Y"/AU OR "HAN R Z"/AU OR "HAN RONG"/AU OR "HAN RONG
                BIN"/AU)
                E BRISSETTE J/AU
L19          26 SEA ABB=ON  PLU=ON  ("BRISSETTE J"/AU OR "BRISSETTE J L"/AU OR
                "BRISSETTE JANICE L"/AU)
                E P21/CT
                E E3+ALL
                E P21 (RHO)PROTEIN/CT
                E E3+ALL
                E E2+ALL
L20        2050 SEA ABB=ON  PLU=ON  RHO GTP-BINDING PROTEINS/CT
                E SIGNAL TRANSDUCTION/CT
                E E3+ALL
L21      171376 SEA ABB=ON  PLU=ON  SIGNAL TRANSDUCTION+NT/CT
                E SIGNAL TRANSDUCTION/CT
                E E5+ALL
                E SIGNAL TRANSDUCTION/CT
                E E7+ALL
                E PROTEINS (L) SIGNALING+OLD/CT
                E PROTEINS/CT
                E PROTEINS S/CT
                E E95+ALL
                E E2+ALL
L22        1597 SEA ABB=ON  PLU=ON  INTRACELLULAR SIGNALING PEPTIDES AND
                PROTEINS/CT
L23       27550 SEA ABB=ON  PLU=ON  (P21 OR P(2A)21 OR P21 PROTEIN KINASE OR
                P21 SIGNAL TRANSDUCT?)
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     (FILE 'HOME' ENTERED AT 12:45:45 ON 28 APR 2006)

     FILE 'CAPLUS' ENTERED AT 12:45:59 ON 28 APR 2006
                E P21/CT
                E E3+ALL
                E E3+ALL
                E P21/CT
                E E8+ALL
                E P21-ACTIVATED KINASE 1/CT
                E E3+ALL
L1          658 SEA ABB=ON  PLU=ON  P21-ACTIVATED KINASE/CT
                E P21/CT
                E E3+ALL
L2            0 SEA ABB=ON  PLU=ON  PROTEINS (L) P21/CT
                E SIGNAL TRANSDUCTION/CT
                E E4+ALL
                E SIGNAL TRANSDUCTION/CT
                E E5+ALL
                E E2+ALL
L3            0 SEA ABB=ON  PLU=ON  PROTEINS (L) SIGNALING+OLD/CT
                E SIGNAL TRANSDUCTION/CT
                E E6+ALL
                E SIGNAL TRANSDUCTION/CT
                E E9+ALL
L4       142893 SEA ABB=ON  PLU=ON  SIGNAL TRANSDUCTION/CT
L*** DEL 142893 S SIGNAL TRANSDUCTION, BIOLOGICAL/CT
L*** DEL      0 S L5 NOT L4
L5        88152 SEA ABB=ON  PLU=ON  (P21 OR P(2A)21 OR P21 PROTEIN KINASE OR
                P21 SIGNAL TRANSDUCTION? OR P21?)
                E WRINKLE/CT
                E WRINKLES/CT
                E E1
                E E3+ALL
                E E2+ALL
L6            0 SEA ABB=ON  PLU=ON  COSMETICS (L) CREAMS, WRINKLE-PREVENTING/CT

                E WRINKLES/CT
                E E2+ALL
                E E2+ALL
                E SKIN AGIN/CT
                E E4+ALL
                E E2+ALL
                E SKIN WRINKL/CT
L7        11170 SEA ABB=ON  PLU=ON  (WRINKL? OR SKIN WRINKL? OR WRINK? REDUC?)

L8           25 SEA ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4 OR L5) AND L7

     FILE 'STNGUIDE' ENTERED AT 13:01:54 ON 28 APR 2006

     FILE 'CAPLUS' ENTERED AT 13:03:52 ON 28 APR 2006
L9            2 SEA ABB=ON  PLU=ON  L8 AND (P(2A)21)
                D SCAN
                D KWIC
                D KWIC 2

     FILE 'STNGUIDE' ENTERED AT 13:05:43 ON 28 APR 2006
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20. A method of providing a record, the method comprising: providing a test agent; determining whether the test agent increases or induces **p21**; and generating a record that correlates the ability of the test agent to increase expression, activity or levels of **p21** with the agent's ability to reduce the appearance or formation of **wrinkles**, thereby providing a record.

21. A method of providing **wrinkle** protection to a subject, said method comprising: supplying to the subject a composition that increases or induces a component of the a **p21** signal transduction pathway; and supplying to the subject instructions for using said composition to prevent or reduce **wrinkles.**

22. The method of claim 20, wherein the component of the a **p21** signal transduction pathway is **p21.**

25. A kit for preventing **wrinkles** in a subject, said kit comprising: a composition comprising an agent that increases or induces a component of the **p21** signal transduction pathway; and instructions for using the composition to prevent **wrinkles.**

26. The kit of claim 25, wherein said component of the a **p21** signal transduction pathway is **p21.**

IT **Skin**, disease
(**aging**, **wrinkles**; methods and compns. for preventing skin damage)
IT Proteins
(**p21**; methods and compns. for preventing skin damage)

=>

and/or reduce UVB-induced skin damage, e.g., **wrinkles.** The method includes identifying an agent that increases or induces the expression, activity or levels of a component of the **p21** signal transduction pathway. Also included are methods and compositions for treating UVB-induced skin damage.

CLM What is claimed is:

1. A method of screening for an agent that reduces the appearance or formation of **wrinkles**, the method comprising: providing a test agent; determining whether the test agent increases or induces a component of the **p21** signal transduction pathway; and correlating the ability of a test agent to increase expression, activity or levels of a component of the **p21** signal transduction pathway with the agent's ability to reduce the appearance or formation of **wrinkles**, thereby screening for an agent that reduces the appearance or formation of **wrinkles.**

2. The method of claim 1, further comprising evaluating the effect of the agent on **wrinkles** on the skin of a subject.

3. The method of claim 1, further comprising selecting a test agent that increases expression, activity or levels of a component of the **p21** signal transduction.

4. The method of claim 1, wherein the determining step comprises determining if the test agent increases or induces **p21.**

6. The method of claim 1, wherein the determining step comprises: (a) providing a cell, tissue or non-human subject comprising an exogenous nucleic acid comprising a regulatory region of a component of the **p21** signal transduction pathway operably linked to a nucleotide sequence encoding a reporter polypeptide; and (b) evaluating the ability of the test agent to increase the activity of the reporter polypeptide in the cell, tissue or non-human subject, wherein the test agent is determined to increase or induce a component of the **p21** signal transduction pathway if it increases the activity of the reporter polypeptide.

7. The method of claim 4, wherein the determining step comprises: (a) providing a cell, tissue or non-human subject comprising an exogenous nucleic acid comprising a **p21** regulatory region operably linked to a nucleotide sequence encoding a reporter polypeptide; and (b) evaluating the ability of the test agent to increase the activity of the reporter polypeptide in the cell, tissue or non-human subject, wherein the test agent is determined to increase or induce **p21** if it increases the activity of the reporter polypeptide.

11. The method of claim 2, wherein the effect of the agent on UVB-induced **wrinkles** is evaluated.

12. A method of preventing or treating **wrinkles**, the method comprising: (a) identifying a subject in need of prevention or treatment of **wrinkles**; and (b) administering to the subject an agent that increases or induces a component of the **p21** signal transduction pathway.

14. The method of claim 12, wherein the component of the **p21** signal transduction pathway is **p21.**

16. A cosmetic composition comprising an agent that increases or induces **p21.**

IT Interferons
RL: BIOL (Biological study)
(α2-, gene for, of human, conformation **wrinkle** in regulatory region of)
IT 9002-64-6 9002-72-6 66796-54-1
RL: PRP (Properties)
(gene for, of cattle and human, conformational **wrinkle** in regulatory region of)
IT 9004-10-8, biological studies
RL: BIOL (Biological study)
(gene for, of dog, conformational **wrinkle** in regulatory region of)
IT 9000-90-2
RL: PRP (Properties)
(gene for, of mouse, conformational **wrinkle** in regulatory region of)
IT 74749-30-7
RL: PRP (Properties)
(gene for, of rat, conformational **wrinkle** in regulatory region of)

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L100 ANSWER 1 OF 1 USPATFULL on STN
ACCESSION NUMBER: 2004:144539 USPATFULL
TITLE: Methods and compositions for preventing skin damage
INVENTOR(S): Fujii, Seishiro, Boston, MA, UNITED STATES
Dotto, Paolo, Boston, MA, UNITED STATES
Han, Rong, Boston, MA, UNITED STATES
Brissette, Janice, Charlestown, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004110203	A1	20040610
APPLICATION INFO.:	US 2003-664795	A1	20030919 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-412503P	20020920 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FISH & RICHARDSON PC, 225 FRANKLIN ST, BOSTON, MA, 02110
NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
LINE COUNT: 649
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention features methods of screening for compounds that prevent and/or reduce UVB-induced skin damage, e.g., **wrinkles.** The method includes identifying an agent that increases or induces the expression, activity or levels of a component of the **p21** signal transduction pathway. Also included are methods and compositions for treating UVB-induced skin damage.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention features methods of screening for compounds that prevent

RL: PRP (Properties)
(gene for, of rat, conformational **wrinkle** in regulatory region of)

IT Ribonucleic acids, ribosomal
RL: BIOL (Biological study)
(gene for, of Xenopus laevis, conformational **wrinkle** in regulatory region of)

IT Eukaryote
(genes of, conformational **wrinkle** in regulatory region of)

IT Gene and Genetic element, animal
RL: BIOL (Biological study)
(of eukaryotes, conformational **wrinkle** in regulatory region of)

IT Conformation and Conformers
(of **wrinkle**, in eukaryote gene regulatory region)

IT Histones
RL: BIOL (Biological study)
(H1, gene for, of sea urchin, conformational **wrinkle** in regulatory region of)

IT Histones
RL: BIOL (Biological study)
(H4, gene for, of sea urchin, conformational **wrinkle** in regulatory region of)

IT Metallothioneins
RL: BIOL (Biological study)
(II, gene for, of human, conformation **wrinkle** in regulatory region of)

IT Virus, animal
(Moloney murine leukemia, genes of, conformational **wrinkle** in regulatory region of)

IT Proteins
RL: BIOL (Biological study)
(**P21**, gene for, of Harvey murine sarcoma virus, conformational **wrinkle** in regulatory region of)

IT Ribonucleic acids
RL: BIOL (Biological study)
(U1, gene for, of human, conformation **wrinkle** in regulatory region of)

IT Virus, animal
(adeno-, genes of, conformational **wrinkle** in regulatory region of)

IT Ribonucleic acids, transfer
RL: BIOL (Biological study)
(aspartic acid-specific, gene for, of rat, conformational **wrinkle** in regulatory region of)

IT Ribonucleic acids, transfer
RL: BIOL (Biological study)
(glycine-specific, gene for, of rat, conformational **wrinkle** in regulatory region of)

IT Virus, animal
(herpes simplex, genes of, conformational **wrinkle** in regulatory region of)

IT Proteins
RL: BIOL (Biological study)
(steroid-binding, gene for, of rat prostate, conformational **wrinkle** in regulatory region of)

IT Gene and Genetic element, animal
RL: BIOL (Biological study)
(Y, of chicken, conformational **wrinkle** in regulatory region of)

osteoporosis: bone disease
Osteoporosis (MeSH)
INDEX TERMS: Diseases
skin atrophy: integumentary system disease
INDEX TERMS: Chemicals & Biochemicals
Brca1: full-length isoform; **p21**; p53
INDEX TERMS: Miscellaneous Descriptors
aging; body fat deposition; malignant transformation; senescence; tumorigenesis
ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse (common): adult
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

L115 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:608001 CAPLUS
DOCUMENT NUMBER: 103:208001
TITLE: Structural **wrinkles** and the genomic regulatory sites of eukaryotes
AUTHOR(S): Nussinov, Ruth
CORPORATE SOURCE: Lab. Mol. Genet., Natl. Inst. Child Health Hum. Dev., Bethesda, MD, 20205, USA
SOURCE: Journal of Molecular Evolution (1985), 22(2), 150-9
CODEN: JMEVAU; ISSN: 0022-2844
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 28 Dec 1985
AB Calcns. of DNA angular parameters in 50 eukaryotic sequences reveal regions of large conformational deviations from ideal DNA around regulatory sites. Frequently, discrete peaks of structural variation are present upstream of genes. Known regulatory regions often include variants of consensus sequences. Thus, imprecise sequences and structures are recognized within large genomic stretches. The existence of structurally **wrinkled** regions in the vicinity of regulatory sequences is likely to facilitate greatly their recognition by proteins and enzymes.
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 6, 10, 12, 13
IT Immunoglobulins
RL: BIOL (Biological study)
(gene for κ chain of, of mouse, conformational **wrinkle** in regulatory region of)
IT Keratins
Ovalbumins
RL: BIOL (Biological study)
(gene for, of chicken, conformational **wrinkle** in regulatory region of)
IT Globulins
RL: BIOL (Biological study)
(gene for, of eukaryote, conformation **wrinkle** in regulatory region of)
IT Actins

REGISTRY NUMBER: 9001-12-1 (matrix metalloproteinase-1)
60-40-2 (mecamylamine)
54-11-5 (nicotine)
260524-81-0 (GenBank-AB040450)
279212-93-0 (GenBank-AB043585)
136218-12-7 (GenBank-M37981)
384427-81-0 (GenBank-M64349)
140831-43-2 (GenBank-M83712)
384591-99-5 (GenBank-U13737)
171752-05-9 (GenBank-U40583)
174387-61-2 (GenBank-U48861)
391554-91-9 (GenBank-U62437)

L115 ANSWER 10 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:88211 BIOSIS
DOCUMENT NUMBER: PREV200300088211
TITLE: Senescence, aging, and malignant transformation mediated by p53 in mice lacking the Brca1 full-length isoform.
AUTHOR(S): Cao, Liu; Li, Wenmei; Kim, Sangsoo; Brodie, Steven G.; Deng, Chu-Xia [Reprint Author]
CORPORATE SOURCE: Genetics of Development and Diseases Branch, National Institutes of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892, USA
chuxiad@bdg10.niddk.nih.gov
SOURCE: Genes & Development, (January 15 2003) Vol. 17, No. 2, pp. 201-213. print.
CODEN: GEDEEP. ISSN: 0890-9369.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Feb 2003
Last Updated on STN: 12 Feb 2003
ABSTRACT:Senescence may function as a two-edged sword that brings unexpected consequences to organisms. Here we provide evidence to support this theory by showing that the absence of the Brca1 full-length isoform causes senescence in mutant embryos and cultured cells as well as **aging** and tumorigenesis in adult mice. Haploid loss of p53 overcame embryonic senescence but failed to prevent the adult mutant mice from prematurely **aging**, which included decreased life span, reduced body fat deposition, osteoporosis, **skin** atrophy, and decreased wound healing. We further demonstrate that mutant cells that escaped senescence had undergone clonal selection for faster proliferation and extensive genetic/molecular alterations, including overexpression of cyclin D1 and cyclin A and loss of p53. These observations provide the first in vivo evidence that links cell senescence to **aging** due to impaired function of Brca1 at the expense of tumorigenesis.
CONCEPT CODE: Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Bones, joints, fasciae, connective and adipose tissue - Pathology 18006
Integumentary system - Pathology 18506
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Gerontology 24500
INDEX TERMS: Major Concepts
Aging; Biochemistry and Molecular Biophysics; Tumor Biology
INDEX TERMS: Diseases
decreased wound healing: integumentary system disease
INDEX TERMS: Diseases

functioning, leading to changes in **skin** homeostasis. Using RT-PCR and Western blotting, we found that a 24-hour exposure of human DF to 10 muM Nic causes a 1.9- to 28-fold increase of the mRNA and protein levels of the cell cycle regulators **p21**, cyclin D1, Ki-67, and PCNA and a 1.7- to 2-fold increase of the apoptosis regulators Bcl-2 and caspase 3. Nic exposure also up-regulated expression of the dermal matrix proteins collagen type lalpha1 and elastin as well as matrix metalloproteinase-1. Mecamylamine (Mec), the specific antagonist of nAChRs, abolished Nic-induced alterations, indicating that they resulted from a pharmacologic stimulation of nAChRs expressed by DF. To establish the relevance of these findings to a specific nicotinergic pathway, we studied human DF transfected with anti-alpha3 antisense oligonucleotides and murine DF from alpha3 nAChR knockout mice. In both cases, lack of alpha3 was associated with alterations in fibroblast growth and function that were opposite to those observed in DF treated with Nic, suggesting that the nicotinic effects on DF were mostly mediated by alpha3 nAChR. In addition to alpha3, the nAChR subunits detected in human DF were alpha5, alpha7, beta2, and beta4. The exposure of DF to Nic altered the relative amounts of each of these subunits, leading to reciprocal changes in (3H)epibatidine-binding kinetics. Thus, some of the pathobiologic effects of tobacco products on extracellular matrix turnover in the **skin** may stem from Nic-induced alterations in the physiologic control of the unfolding of the genetically determined program of growth and the tissue remodeling function of DF as well as alterations in the structure and function of fibroblast nAChRs.

CONCEPT CODE: Cytology - Animal 02506
Biochemistry studies - General 10060
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064
Integumentary system - Physiology and biochemistry 18504
Toxicology - General and methods 22501

INDEX TERMS: Major Concepts
Toxicology

INDEX TERMS: Parts, Structures, & Systems of Organisms
dermal fibroblast: integumentary system; skin: integumentary system

INDEX TERMS: Chemicals & Biochemicals
Ki-67; PCNA; [tritiated hydrogen]epibatidine; alpha-3 nicotinic acetylcholine receptor; anti-alpha-3 antisense oligonucleotides; collagen type 1; cyclin D1; elastin; matrix metalloproteinase-1; mecamylamine; nicotine: toxicity; nicotinic acetylcholine receptors; **p21**

INDEX TERMS: Sequence Data
AB040450: GenBank, nucleotide sequence; AB043585: GenBank, nucleotide sequence; JO4038: nucleotide sequence; M37981: GenBank, nucleotide sequence; M64349: GenBank, nucleotide sequence; M83712: GenBank, nucleotide sequence; NM-000088: nucleotide sequence; NM-000501: nucleotide sequence; NM-002421: nucleotide sequence; NM-138578: nucleotide sequence; U13737: GenBank, nucleotide sequence; U40583: GenBank, nucleotide sequence; U48861: GenBank, nucleotide sequence; U62437: GenBank, nucleotide sequence

INDEX TERMS: Methods & Equipment
RT-PCR: genetic techniques, laboratory techniques; Western blotting: genetic techniques, laboratory techniques

INDEX TERMS: Miscellaneous Descriptors
tobacco products

Integumentary system - Physiology and biochemistry 18504
Integumentary system - Pathology 18506
INDEX TERMS: Major Concepts
Integumentary System (Chemical Coordination and Homeostasis)
INDEX TERMS: Parts, Structures, & Systems of Organisms
epidermal cell: integumentary system
INDEX TERMS: Diseases
seborrheic keratosis: integumentary system disease, pathology
Keratosis, Seborrheic (MeSH)
INDEX TERMS: Chemicals & Biochemicals
DNA; cyclin A: expression; cyclin D: expression; cyclin E: expression; p16: expression; **p21: expression** ; p53: expression; retinoblastoma protein: expression; telomerase-associated protein 1 [TP1]
INDEX TERMS: Miscellaneous Descriptors
DNA fragmentation; G-1 arrest; survival time
ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common)
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L115 ANSWER 9 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:141899 BIOSIS
DOCUMENT NUMBER: PREV200300141899
TITLE: Central role of fibroblast alpha3 nicotinic acetylcholine receptor in mediating cutaneous effects of nicotine.
AUTHOR(S): Arredondo, Juan; Hall, Leon L.; Ndoye, Assane; Nguyen, Vu Thuong; Chernyavsky, Alexander I.; Bercovich, Dani; Orr-Urtreger, Avi; Beaudet, Arthur L.; Grando, Sergei A. [Reprint Author]
CORPORATE SOURCE: Department of Dermatology, University of California Davis Medical Center, 4860 Y Street, Suite 3400, Sacramento, CA, 95817, USA
sagrando@ucdavis.edu
SOURCE: Laboratory Investigation, (February 2003) Vol. 83, No. 2, pp. 207-225. print.
CODEN: LAINAW. ISSN: 0023-6837.
DOCUMENT TYPE: Article
LANGUAGE: English
OTHER SOURCE: GenBank-AB040450; GenBank-AB043585; GenBank-M37981; GenBank-M64349; GenBank-M83712; GenBank-U13737; GenBank-U40583; GenBank-U48861; GenBank-U62437
ENTRY DATE: Entered STN: 19 Mar 2003
Last Updated on STN: 9 May 2003
ABSTRACT:Smoking is associated with aberrant cutaneous tissue remodeling, such as precocious **skin aging** and impaired wound healing. The mechanism is not fully understood. Dermal fibroblasts (DF) are the primary cellular component of the dermis and may provide a target for pathobiologic effects of tobacco products. The purpose of this study was to characterize a mechanism of nicotine (Nic) effects on the growth and tissue remodeling function of DF. We hypothesized that the effects of Nic on DF result from its binding to specific nicotinic acetylcholine receptors (nAChRs) expressed by these cells and that downstream signaling from the receptors alters normal cell

Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
REGISTRY NUMBER: 9031-11-2 (beta-galactosidase)
9031-11-2 (EC 3.2.1.23)
7440-47-3 (chromium)

L115 ANSWER 8 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:547465 BIOSIS
DOCUMENT NUMBER: PREV200300549209
TITLE: Enhanced expression of p 6 in seborrhoeic keratosis; a lesion of accumulated senescent epidermal cells in G1 arrest.
AUTHOR(S): Nakamura, S. [Reprint Author]; Nishioka, K.
CORPORATE SOURCE: Department of Environmental Immunodermatology, Tokyo Medical and Dental University, Graduate School, Yushima 1-5-45, Bunkyoku, Tokyo, 113-8519, Japan
ruggle@mbk.sphere.ne.jp
SOURCE: British Journal of Dermatology, (September 2003) Vol. 149, No. 3, pp. 560-565. print.
CODEN: BJDEAZ. ISSN: 0007-0963.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Nov 2003
Last Updated on STN: 19 Nov 2003
ABSTRACT:Background Seborrhoeic keratosis (SK) is a common **skin** disease associated with **skin ageing** and photoageing, but only limited studies have been performed on SK and the senescence of keratinocytes. Objectives We sought to clarify the genetic basis of SK and the senescence of keratinocytes. Methods Expression of p16, cyclins A, D and E, ***p21*** , p53, retinoblastoma (Rb) gene product and telomerase-associated protein 1 (TP1) in SK was examined by immunohistochemistry. DNA fragmentation in SK was detected by the terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate-biotin nick end labelling method. We cultured keratinocytes from SK lesions and non-lesional epidermis and examined expression of p16, observed morphology of the cultured cells by light and electron microscopy and measured survival time. Results p16, a cyclin-dependent kinase inhibitor, was expressed in all cells from SK lesions, whereas normal keratinocytes expressed p16 only in the granular cells. Other factors such as cyclins A, D and E, **p21**, p53, Rb gene product, and TP1, were not expressed in SK cells. These results suggest that p1 6 expression is a marker of SK and that p16 has a role in the pathogenesis of SK. DNA fragmentation was not detected in four of five SK tissue samples; one of the SK tissue samples showed DNA fragmentation only in the superficial upper layer of an SK lesion, suggesting that apoptosis was inhibited in SK cells. In contrast, normal epidermis showed DNA fragmentation in the granular and squamous layers. Immunohistochemical examination of cultured SK cells also revealed the presence of p16. A greater number of SK cells survived after 3 weeks of culture in comparison with normal keratinocytes. Features of senescence, such as a balloon-like appearance after lengthy culture and increased amounts of tonofilaments in cytoplasm, were observed in SK cells in culture. Conclusions These results suggest that SK is a benign neoplasm where keratinocytes in a senescent condition and G1 arrest are accumulated.
CONCEPT CODE: Cytology - Animal 02506
Cytology - Human 02508
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Biochemistry studies - Proteins, peptides and amino acids 10064
Pathology - General 12502

1079-1087. print.
ISSN: 0531-5565 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Nov 2004
Last Updated on STN: 24 Nov 2004

ABSTRACT:Heavy metals like CrVI, CdII, PbII and Still have many applications in industry. They also represent a group of labour pollutants, as they are involved in several physiological disorders, such as carcinogenesis and various tissue dysfunctions. However, limited knowledge exists regarding their effects on **ageing.** In the current work we provide evidence that workers chronically exposed to CrVI have considerably reduced serum levels of the biomarker of senescence and cell survival, Apolipoprotein J/Clusterin (ApoJ/CLU). Moreover, we have found that both the degree and the time of exposure to CrVI associate negatively with ApoJ/CLU serum levels. To further examine whether CrVI directly affects cellular senescence we treated for 10 weeks two adult **skin** fibroblasts cultures as well as embryonic fibroblasts with a range of CrVI concentrations that approximate the values recorded in the blood circulation of exposed workers. Cellular treatment with a CrVI concentration that approximates the highest concentration in the blood was extremely toxic and nearly all cells died immediately after the first treatment. Interestingly, continuous treatment with a 10-fold lower CrVI concentration resulted in the induction of premature senescence. More specifically, treated cells were growth arrested, acquired an irregular shape, were positive to P-galactosidase staining, accumulated oxidized proteins and over-expressed the cyclin-dependent kinase inhibitor **p21** and ApoJ/CLU. Similar treatments with three additional tabour pollutants resulted in the induction of premature senescence by CdII, but not by Still or PbII. In summary, our results indicate that exposure to CrVI induces alterations of senescence biomarkers both in vivo and in vitro. They also provide new valuable tools for monitoring CrVI cytotoxic effects in vivo as well as for re-evaluating the maximum permissive values of some labour pollutants, like CrVI and CdII.

CONCEPT CODE: Biochemistry studies - General 10060
Biochemistry studies - Minerals 10069
Enzymes - General and comparative studies: coenzymes 10802
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Gerontology 24500
Public health - Occupational health 37013
INDEX TERMS: Major Concepts
Aging; Biochemistry and Molecular Biophysics; Occupational Health (Allied Medical Sciences)
INDEX TERMS: Parts, Structures, & Systems of Organisms
serum: blood and lymphatics
INDEX TERMS: Chemicals & Biochemicals
apolipoprotein J; beta-galactosidase [EC 3.2.1.23]; biomarkers; chromium; clusterin; cyclin-dependent kinase inhibitor; heavy metal; labour pollutants; **p21**
INDEX TERMS: Methods & Equipment
staining: laboratory techniques
INDEX TERMS: Miscellaneous Descriptors
aging; cell survival; cellular senescence
ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common): adult, male

of environmental toxins including solar radiation comprising applying (C);

(3) treating skin inflammatory conditions arising from stimuli such as exposure to allergies, solar radiation or skin infection comprising applying to cells (C);

(4) increasing cell mass comprises applying to cells (C); and

(5) a pharmaceutical composition comprising (C) in combination with a pharmaceutically acceptable carrier.

ACTIVITY - Antiinflammatory; antiageing.

Acetyl-carnosine was shown to markedly delay the onset of senescence of cells by increasing the lifespan of MRC-5 cells in culture. This was confirmed by rejuvenation experiments. The morphology of cells grown in media supplemented with acetyl-carnosine was distinct from the controls. In control flasks cells were broad and flat with long processes extending to other cells. In fact some cells began to extend bipolar processes. Cells became very granular and debris accumulated in the medium. This morphology was typical of senescent cells. However, cells grown in media supplemented with acetyl-carnosine were long and spindle and gave an appearance of steaming. Cell growth showed confluency and cells acquired a phenotype typical of younger cells. To confirm this rejuvenation of senescent cells by acetyl-carnosine the expression of 3 known biomarkers used were **p21**, p27 and p16 and are all cyclin-dependent kinase inhibitors and are expressed at different stages of the cell cycle. In both cases non-senescent cultures show about a 30% of nuclei unstained while essentially all nuclei stain in senescent cultures. Once cells started to exhibit some degree of nuclei staining indicating senescence, old media was replaced with media supplemented with acetyl-carnosine, and after a few days, cells began to adopt a younger phenotype and there was no expression of p16 in the nucleus.

MECHANISM OF ACTION - None given.

USE - The novel method is used for altering the senescence of cells, and in the preparation of medicament for treating aging, degenerative-related diseases, slowing down aging of skin and skin inflammatory conditions (claimed).

ADVANTAGE - N-acetyl carnosine has superior anti-ageing properties than prior use of L-carnosine. Longevity growth curves showed that N-acetyl carnosine allowed more population doublings (PDs) than controls and significantly more PDs than carnosine itself. In addition, N-acetyl carnosine was found to be almost completely resistant to attack by human blood peptidases.

Dwg.0/0

TECH UPTX: 20020618

TECHNOLOGY FOCUS - BIOLOGY - Preferred Cells: The cells are human fibroblast cells, such as human fetal lung fibroblasts.

L115 ANSWER 7 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:453400 BIOSIS

DOCUMENT NUMBER: PREV200400452193

TITLE: Alterations of senescence biomarkers in human cells by exposure to CrVI in vivo and in vitro.

AUTHOR(S): Katsiki, Magda; Trougakos, loarmis P.; Chondrogianni, Niki; Alexopoulos, Evangelos C.; Makropoulos, Vassilis; Gonos, Efstathios S. [Reprint Author]

CORPORATE SOURCE: Lab Mol and Cellular AgeingInst Biol Res and Biotechnol, Natl Hellen Res Fdn, 48 Vas Constantinou Ave, Athens, 11635, Greece
sgonos@eie.gr

SOURCE: Experimental Gerontology, (July 2004) Vol. 39, No. 7, pp.

which characterize **skin aging** including skin texture, changes in pigmentation or discoloration, disminution of immunoreactiveness, increased sensitivity to toxic and genotoxic effects of environmental toxins including solar radiation comprising applying (C);

(3) treating skin inflammatory conditions arising from stimuli such as exposure to allergies, solar radiation or skin infection comprising applying to cells (C);

(4) increasing cell mass comprises applying to cells (C); and

(5) a pharmaceutical composition comprising (C) in combination with a pharmaceutically acceptable carrier.

ACTIVITY - Antiinflammatory; antiageing.

Acetyl-carnosine was shown to markedly delay the onset of senescence of cells by increasing the lifespan of MRC-5 cells in culture. This was confirmed by rejuvenation experiments. The morphology of cells grown in media supplemented with acetyl-carnosine was distinct from the controls. In control flasks cells were broad and flat with long processes extending to other cells. In fact some cells began to extend bipolar processes. Cells became very granular and debris accumulated in the medium. This morphology was typical of senescent cells. However, cells grown in media supplemented with acetyl-carnosine were long and spindle and gave an appearance of steaming. Cell growth showed confluency and cells acquired a phenotype typical of younger cells. To confirm this rejuvenation of senescent cells by acetyl-carnosine the expression of 3 known biomarkers used were **p21**, p27 and p16 and are all cyclin-dependent kinase inhibitors and are expressed at different stages of the cell cycle. In both cases non-senescent cultures show about a 30% of nuclei unstained while essentially all nuclei stain in senescent cultures. Once cells started to exhibit some degree of nuclei staining indicating senescence, old media was replaced with media supplemented with acetyl-carnosine, and after a few days, cells began to adopt a younger phenotype and there was no expression of p16 in the nucleus.

MECHANISM OF ACTION - None given.

USE - The novel method is used for altering the senescence of cells, and in the preparation of medicament for treating aging, degenerative-related diseases, slowing down aging of skin and skin inflammatory conditions (claimed).

ADVANTAGE - N-acetyl carnosine has superior anti-ageing properties than prior use of L-carnosine. Longevity growth curves showed that N-acetyl carnosine allowed more population doublings (PDs) than controls and significantly more PDs than carnosine itself. In addition, N-acetyl carnosine was found to be almost completely resistant to attack by human blood peptidases.

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B07-D09; B14-C03; B14-N17
AN 2002-352125 [38] WPIX
AB WO 200226940 A UPAB: 20020618

NOVELTY - Altering the senescence of cells, or a combination of delaying the onset, preventing or reversing the senescence of cells, comprising applying to cells a composition (C) that includes N-acetyl-carnosine as an active ingredient, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) treating aging or degenerative related diseases in a subject, comprises applying to cells (C);

(2) slowing down aging of skin and the development of those features which characterize **skin aging** including skin texture, changes in pigmentation or discoloration, disminution of immunoreactiveness, increased sensitivity to toxic and genotoxic effects

in human fibroblasts. However, their inactivation may enhance the probability of spontaneous immortalization.

CONTROLLED TERM: *Cell Aging: PH, physiology
Cyclin-Dependent Kinase Inhibitor p21
*Cyclins: ME, metabolism
Fibroblasts: ME, metabolism
*Fibroblasts: PH, physiology
Humans
Li-Fraumeni Syndrome: ME, metabolism
*Li-Fraumeni Syndrome: PA, pathology
Research Support, U.S. Gov't, P.H.S.
Tumor Suppressor Protein p53: ME, metabolism

CHEMICAL NAME: 0 (CDKN1A protein, human); 0 (Cyclin-Dependent Kinase Inhibitor **p21**); 0 (Cyclins); 0 (Tumor Suppressor Protein p53)

L115 ANSWER 6 OF 13 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
AN 2002-352125 [38] WPIX
DNC C2002-100114
TI Altering the senescence of cells for treating aging, degenerative-related diseases or skin allergies, comprises application of a composition of N-acetyl-Carnosine.
DC B04
IN GRIGG, G W; MALLOY, P; MOLLOY, P
PA (BETA-N) BETA PEPTIDE FOUND PTY LTD; (CSIR) COMMONWEALTH SCI & IND RES ORG; (GRIG-I) GRIGG G W; (MOLL-I) MOLLOY P
CYC 97
PI WO 2002026940 A1 20020404 (200238)* EN 23 C12N005-06
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001093484 A 20020408 (200252) C12N005-06
EP 1328620 A1 20030723 (200350) EN C12N005-06
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 2004014814 A1 20040122 (200407) A61K031-198
ADT WO 2002026940 A1 WO 2001-AU1199 20010925; AU 2001093484 A AU 2001-93484 20010925; EP 1328620 A1 EP 2001-973818 20010925, WO 2001-AU1199 20010925; US 2004014814 A1 WO 2001-AU1199 20010925, US 2003-381057 20030728
FDT AU 2001093484 A Based on WO 2002026940; EP 1328620 A1 Based on WO 2002026940
PRAI AU 2000-382 20000926
IC ICM A61K031-198; C12N005-06
ICS A61K031-4172; A61P017-00; C12N005-08
AB WO 200226940 A UPAB: 20020618
NOVELTY - Altering the senescence of cells, or a combination of delaying the onset, preventing or reversing the senescence of cells, comprising applying to cells a composition (C) that includes N-acetyl-carnosine as an active ingredient, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) treating aging or degenerative related diseases in a subject, comprises applying to cells (C);
(2) slowing down aging of skin and the development of those features

CONTROLLED TERM: Actins: GE, genetics
*Actins: ME, metabolism
Adult
*Aging: ME, metabolism
Cells, Cultured
Cyclin-Dependent Kinase Inhibitor p21
Cyclins: GE, genetics
*Cyclins: ME, metabolism
Epidermis: CY, cytology
Epidermis: EM, embryology
Epidermis: ME, metabolism
Fetus: ME, metabolism
Fibroblasts: CY, cytology
Fibroblasts: ME, metabolism
Humans
Procollagen: GE, genetics
*Procollagen: ME, metabolism
RNA, Messenger: ME, metabolism
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.

CHEMICAL NAME: 0 (Actins); 0 (CDKN1A protein, human); 0 (Cyclin-Dependent Kinase Inhibitor **p21**); 0 (Cyclins); 0 (Procollagen); 0 (RNA, Messenger)

L115 ANSWER 5 OF 13 MEDLINE on STN
ACCESSION NUMBER: 96438605 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8840965
TITLE: Expression of **p21** is not required for senescence of human fibroblasts.
AUTHOR: Medcalf A S; Klein-Szanto A J; Cristofalo V J
CORPORATE SOURCE: Center for Gerontological Research, Medical College of Pennsylvania and Hahnemann University, Philadelphia 19129, USA.
CONTRACT NUMBER: AG00131 (NIA)
AG00378 (NIA)
AG00532 (NIA)
+
SOURCE: Cancer research, (1996 Oct 15) Vol. 56, No. 20, pp. 4582-5.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19 Dec 1996
Last Updated on STN: 19 Dec 1996
Entered Medline: 4 Nov 1996

ABSTRACT:
Senescence and immortalization have been studied in **skin** fibroblasts derived from two individuals with the Li-Fraumeni syndrome. These cells inherit one wild-type and one mutant p53 allele and lose the former during culture. Despite this loss, cultures of Li-Fraumeni syndrome cells progressed normally from early passage to replicative senescence. Senescent cells also expressed barely detectable levels of **p21** mRNA, and, in marked contrast to normal cultured cells, levels of **p21** expression decreased during in vitro **aging.** Further maintenance for up to 10 months of post-mitotic cultures has led to the isolation of cells with an extended lifespan. Four potentially immortal cultures have continued to proliferate, and two have completed more than 110 population doublings. These results indicate that p53 and **p21** are not required for replicative senescence

Transcription Factors: ME, metabolism
Transcription, Genetic
*Tretinoin: PD, pharmacology
Ultraviolet Rays
Up-Regulation
p38 Mitogen-Activated Protein Kinases

CAS REGISTRY NO.: 302-79-4 (Tretinoin)

CHEMICAL NAME: 0 (ATF2 protein, human); 0 (Activating Transcription Factor 2); 0 (Antineoplastic Agents); 0 (Cyclic AMP Response Element-Binding Protein); 0 (Nerve Tissue Proteins); 0 (Proto-Oncogene Proteins c-jun); 0 (Transcription Factor AP-1); 0 (Transcription Factors); EC 2.7.1.112 (Receptor, Epidermal Growth Factor); EC 2.7.1.123 (Ca(2+)-Calmodulin Dependent Protein Kinase); EC 2.7.1.37 (JNK Mitogen-Activated Protein Kinases); EC 2.7.1.37 (Mitogen-Activated Protein Kinases); EC 2.7.1.37 (p38 Mitogen-Activated Protein Kinases); EC 3.6.5.2 (HRAS protein, human); EC 3.6.5.2 (Proto-Oncogene Proteins **p21**(ras))

L115 ANSWER 4 OF 13 MEDLINE on STN

ACCESSION NUMBER: 97370256 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9226632

TITLE: Abundance of alpha 1(I) and alpha 1(III) procollagen and **p21** mRNAs in fibroblasts cultured from fetal and postnatal dermis.

AUTHOR: Furth J J; Allen R G; Tresini M; Keogh B; Cristofalo V J

CORPORATE SOURCE: Center for Gerontological Research, Allegheny University of The Health Sciences, Philadelphia, PA 19129-1191, USA.

CONTRACT NUMBER: AG 00378 (NIA)
AG 00523 (NIA)
AG00131 (NIA)

SOURCE: Mechanisms of ageing and development, (1997 Aug) Vol. 97, No. 2, pp. 131-42.
Journal code: 0347227. ISSN: 0047-6374.

PUB. COUNTRY: Ireland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199709

ENTRY DATE: Entered STN: 22 Sep 1997
Last Updated on STN: 22 Sep 1997
Entered Medline: 11 Sep 1997

ABSTRACT:
The steady-state abundance of alpha 1(I) and alpha 1(III) procollagen mRNAs, p21Sdi1 mRNA, and beta-actin mRNA was determined in 29 **skin** fibroblast lines established from fetal, young and old donors. Donor ages ranged from 12 gestational weeks to nonagenarian. Adult donors were members of the Baltimore Longitudinal Study of **Aging.** The abundance of alpha 1(I) procollagen mRNA was decreased in cell lines from both young and old donors compared with fetal lines. Additionally, one alpha 1(I) transcript observed in the fetal lines was not detected in postnatal lines. The abundance of alpha 1(III) procollagen mRNA was decreased in postnatal lines from old donors compared with fetal lines. The abundance of beta-actin mRNA was lower in postnatal lines from both young and old donors compared to fetal lines. These results suggest that cultures of fetal **skin** fibroblasts exhibit a greater capacity for synthesis of procollagens and beta-actin than postnatal lines. In contrast, the abundance of p21Sdi1 mRNA was elevated in lines established from postnatal donors. These results are consistent with developmental changes in amounts of procollagen, beta-actin and **p21.**

Entered Medline: 23 Apr 1998

ABSTRACT:
Human **skin** is exposed daily to solar ultraviolet (UV) radiation. UV induces the matrix metalloproteinases collagenase, 92-kD gelatinase, and stromelysin, which degrade **skin** connective tissue and may contribute to premature **skin aging** (photoaging). Pretreatment of ***skin*** with all-trans retinoic acid (tRA) inhibits UV induction of matrix metalloproteinases. We investigated upstream signal transduction pathways and the mechanism of tRA inhibition of UV induction of matrix metalloproteinases in human **skin** in vivo. Exposure of human **skin** in vivo to low doses of UV activated EGF receptors, the GTP-binding regulatory protein p21Ras, and stimulated mitogen-activated protein (MAP) kinases, extracellular signal-regulated kinase (ERK), c-Jun amino-terminal kinase (JNK), and p38. Both JNK and p38 phosphorylated, and thereby activated transcription factors c-Jun and activating transcription factor 2 (ATF-2), which bound to the c-Jun promoter and upregulated c-Jun gene expression. Elevated c-Jun, in association with constitutively expressed c-Fos, formed increased levels of transcription factor activator protein (AP) 1, which is required for transcription of matrix metalloproteinases. Pretreatment of human **skin** with tRA inhibited UV induction of c-Jun protein and, consequently, AP-1. c-Jun protein inhibition occurred via a posttranscriptional mechanism, since tRA did not inhibit UV induction of c-Jun mRNA. These data demonstrate, for the first time, activation of MAP kinase pathways in humans in vivo, and reveal a novel posttranscriptional mechanism by which tRA antagonizes UV activation of AP-1 by inhibiting c-Jun protein induction. Inhibition of c-Jun induction likely contributes to the previously reported prevention by tRA of UV induction of AP-1-regulated matrix-degrading metalloproteinases in human **skin.**

CONTROLLED TERM: Activating Transcription Factor 2
*Antineoplastic Agents: PD, pharmacology
Ca(2+)-Calmodulin Dependent Protein Kinase: ME, metabolism
Ca(2+)-Calmodulin Dependent Protein Kinase: PD, pharmacology
Ca(2+)-Calmodulin Dependent Protein Kinase: RE, radiation effects
Cyclic AMP Response Element-Binding Protein: ME, metabolism
Gene Expression
Humans
JNK Mitogen-Activated Protein Kinases
Mitogen-Activated Protein Kinases: ME, metabolism
Mitogen-Activated Protein Kinases: PD, pharmacology
Mitogen-Activated Protein Kinases: RE, radiation effects
Nerve Tissue Proteins: ME, metabolism
Nerve Tissue Proteins: PD, pharmacology
Nerve Tissue Proteins: RE, radiation effects
Promoter Regions (Genetics)
*Proto-Oncogene Proteins c-jun: GE, genetics
*Proto-Oncogene Proteins c-jun: ME, metabolism
Proto-Oncogene Proteins p21(ras): ME, metabolism
Proto-Oncogene Proteins p21(ras): PD, pharmacology
Proto-Oncogene Proteins p21(ras): RE, radiation effects
Receptor, Epidermal Growth Factor: ME, metabolism
Receptor, Epidermal Growth Factor: RE, radiation effects
Research Support, Non-U.S. Gov't
Signal Transduction: GE, genetics
*Skin: DE, drug effects
Skin: ME, metabolism
*Skin: RE, radiation effects
Transcription Factor AP-1: ME, metabolism

the irradiated keratinocytes was 75% at 24 h post-irradiation. Various cytokeratins and transcription factors were up-regulated within 1 h post-irradiation. After 6 h, expression of a variety of genes related to growth regulation (e.g. **p21**(WAF1), notch 4, and smoothened), apoptosis (e.g. caspase 10, hTRIP, and CRAF1), DNA repair (ERCC1, XRCC1), cytokines (e.g. IL-6, IL-13, TGF-beta, and endothelin 2), and cell adhesion (e.g. RhoE, and RhoGDI) were altered in human keratinocytes. These data suggest the changes in a cascade of gene expression in human keratinocytes occurring within 24 h after UVB exposure. Although the roles of these cellular genes after UVB-irradiation remain to be elucidated, microarray analysis may provide a new view of gene expression in epidermal keratinocytes following UVB exposure.

CONTROLLED TERM: Apoptosis
Cell Survival: RE, radiation effects
Cell Transformation, Neoplastic
Cytokines: GE, genetics
DNA Repair
DNA, Complementary
Dose-Response Relationship, Radiation
Endothelins: GE, genetics
*Gene Expression Regulation: RE, radiation effects
Growth Substances: GE, genetics
Humans
Keratin: GE, genetics
Keratinocytes: CY, cytology
Keratinocytes: PH, physiology
*Keratinocytes: RE, radiation effects
Oligonucleotide Array Sequence Analysis
RNA, Messenger: GE, genetics
Research Support, Non-U.S. Gov't
Transcription Factors: GE, genetics
Transcription, Genetic: RE, radiation effects
*Ultraviolet Rays

CAS REGISTRY NO.: 68238-35-7 (Keratin)

CHEMICAL NAME: 0 (Cytokines); 0 (DNA, Complementary); 0 (Endothelins); 0 (Growth Substances); 0 (RNA, Messenger); 0 (Transcription Factors)

L115 ANSWER 3 OF 13 MEDLINE on STN

ACCESSION NUMBER: 1998171532 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9502786

TITLE: Retinoic acid inhibits induction of c-Jun protein by ultraviolet radiation that occurs subsequent to activation of mitogen-activated protein kinase pathways in human skin in vivo.

AUTHOR: Fisher G J; Talwar H S; Lin J; Lin P; McPhillips F; Wang Z; Li X; Wan Y; Kang S; Voorhees J J

CORPORATE SOURCE: Department of Dermatology, University of Michigan Medical School, Ann Arbor, Michigan 48109-0609, USA.. dianemch@umich.edu

SOURCE: The Journal of clinical investigation, (1998 Mar 15) Vol. 101, No. 6, pp. 1432-40.
Journal code: 7802877. ISSN: 0021-9738.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199804

ENTRY DATE: Entered STN: 30 Apr 1998
Last Updated on STN: 15 Oct 2002

genotoxic insults into growth arrest and apoptotic signaling pathways that ultimately determine cell fate. As a result of its complex interactions with cell cycle machinery and response to mutagenic agents, **p21**(WAF1) also has stage-specific roles in epithelial carcinogenesis. Finally, a view is emerging of **p21**(WAF1) as not merely a cyclin-dependent kinase inhibitor, but also as a direct participant in regulating genes involved in growth arrest, senescence, and **aging**, thus providing an additional layer of control over matters of the cell cycle. This review discusses these various roles played by **p21**(WAF1) in cell cycle control, and attempts to relate these to epithelial cell biology, with special emphasis on keratinocytes.

CONTROLLED TERM: Apoptosis: PH, physiology
Cell Cycle: PH, physiology
Cell Division: PH, physiology
Cyclin-Dependent Kinase Inhibitor p21
*Cyclin-Dependent Kinases: AI, antagonists & inhibitors
Cyclins: GE, genetics
*Cyclins: PH, physiology
*Enzyme Inhibitors: PD, pharmacology
Epithelial Cells: PH, physiology
Gene Expression Regulation
Humans
Keratinocytes: PH, physiology
Mouth Mucosa: CY, cytology
Mutagens: PD, pharmacology
Neoplasms: PA, pathology
Skin: CY, cytology

CHEMICAL NAME: 0 (CDKN1A protein, human); 0 (Cyclin-Dependent Kinase Inhibitor **p21**); 0 (Cyclins); 0 (Enzyme Inhibitors); 0 (Mutagens); EC 2.7.1.37 (Cyclin-Dependent Kinases)

L115 ANSWER 2 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2001490518 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11532376
TITLE: Expression profiling of cancer-related genes in human keratinocytes following non-lethal ultraviolet B irradiation.
AUTHOR: Murakami T; Fujimoto M; Ohtsuki M; Nakagawa H
CORPORATE SOURCE: Department of Dermatology, Jichi Medical School, 3311-1 Yakushiji, Minamikawachi-machi, Kawachi-gun, Tochigi 329-0498, Japan.. takmu@jichi.ac.jp
SOURCE: Journal of dermatological science, (2001 Oct) Vol. 27, No. 2, pp. 121-9.
Journal code: 9011485. ISSN: 0923-1811.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 5 Sep 2001
Last Updated on STN: 29 Oct 2001
Entered Medline: 25 Oct 2001

ABSTRACT:
Ultraviolet B irradiation initiates and promotes **skin** cancers, ***photo*** -**aging**, and immune suppression. In order to elucidate the effect of these processes at the level of gene expression, we used cDNA microarray technology to examine the effect of ultraviolet B irradiation on 588 cancer-related genes in human keratinocytes at 1, 6, and 24 h post-irradiation with a mildly cytotoxic dose of ultraviolet B (170 mJ/cm(2)). The viability of

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PROCESSING COMPLETED FOR L113
PROCESSING COMPLETED FOR L114
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L115 13 DUP REM L109-L114 (0 DUPLICATES REMOVED)
ANSWERS '1-5' FROM FILE MEDLINE
ANSWER '6' FROM FILE WPIX
ANSWERS '7-10' FROM FILE BIOSIS
ANSWER '11' FROM FILE CAPLUS
ANSWER '12' FROM FILE USPATFULL
ANSWER '13' FROM FILE BIOTECHNO

=> d iall 1-5;d all abs abeq tech 6;d iall 7-10;d ibib ed abs hitind 11; d ibib ed abs hitind 12;d iall 13

L115 ANSWER 1 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2002736836 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12499239
TITLE: P21Waf1 control of epithelial cell cycle and cell fate.
AUTHOR: Weinberg Wendy C; Denning Mitchell F
CORPORATE SOURCE: Laboratory of Immunobiology, Division of Monoclonal Antibodies, Center for Biologics Evaluation and Research, FDA, NIH Bldg 29B, Room 3NN04, HFM-564, Bethesda, MD 20892, USA.. weinberg@cber.fda.gov
SOURCE: Critical reviews in oral biology and medicine : an official publication of the American Association of Oral Biologists, (2002) Vol. 13, No. 6, pp. 453-64. Ref: 143
Journal code: 9009999. ISSN: 1045-4411.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Dental Journals; Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 27 Dec 2002
Last Updated on STN: 31 Mar 2003
Entered Medline: 28 Mar 2003
ABSTRACT:
As a broad-acting cyclin-dependent kinase inhibitor, **p21**(WAF1) occupies a central position in the cell cycle regulation of self-renewing tissues such as oral mucosa and **skin.** In addition to regulating normal cell cycle progression decisions, **p21**(WAF1) integrates

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=> file pascal biotechno esbiobase toxcenter kosmet scisearch

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=> d que l97

L92        45765 SEA (P21 OR P 21)
L93        14267 SEA (WRINKL? OR PHOTOAG? OR SKIN (2A)(AGING OR AGEING))
L94           30 SEA L92 AND L93
L95           11 DUP REM L94 (19 DUPLICATES REMOVED)
L97            1 SEA L95 AND DRUG EFFECT/CT


=> s l97

'CT' IS NOT A VALID FIELD CODE
'CT' IS NOT A VALID FIELD CODE
L114           1 L97

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FILE 'HOME' ENTERED AT 16:51:52 ON 28 APR 2006

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L*** HAS NO ANSWERS
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L*** HAS NO ANSWERS
DUPLICATE IS NOT AVAILABLE IN 'KOSMET'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
'1' ANSWERS REMOVED DUE TO ANSWER OVERLAP
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                AND L7
L101          2 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND (P21 OR P 21)



L11         356 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("FUJII S"/AU OR "FUJII
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L12          13 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("DOTTO P"/AU OR "DOTTO P
                DEL"/AU OR "DOTTO PAOLA"/AU OR "DOTTO PAOLO"/AU OR "DOTTO
                PAOLO DEL"/AU)
L13         154 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("HAN R"/AU OR "HAN R D"/AU OR
                "HAN R F"/AU OR "HAN R J"/AU OR "HAN R K W"/AU OR "HAN R M"/AU
                OR "HAN R N N"/AU OR "HAN R P"/AU OR "HAN R Q"/AU OR "HAN R
                S"/AU OR "HAN R T"/AU OR "HAN R X"/AU OR "HAN R Y"/AU OR "HAN
                RONG"/AU OR "HAN RONG BI"/AU OR "HAN RONG BIN"/AU OR "HAN RONG
                DI"/AU OR "HAN RONG DIAN"/AU OR "HAN RONG JIANG"/AU OR "HAN
                RONG RONG"/AU)
L14          29 SEA FILE=CAPLUS ABB=ON  PLU=ON  ("BRISSETTE J"/AU OR "BRISSETTE
                 JANICE"/AU OR "BRISSETTE JANICE L"/AU OR "BRISSETTE JANICE
                LYNN"/AU)
L56           8 SEA FILE=CAPLUS ABB=ON  PLU=ON  SKIN, DISEASE (L) AGING+OLD/CT

L57           0 SEA FILE=CAPLUS ABB=ON  PLU=ON  PHOTO AGING/CT
L58        5521 SEA FILE=CAPLUS ABB=ON  PLU=ON  (SKIN OR PHOTO) (L) (AGING OR
                AGEING)
L61           6 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L56 OR L57 OR L58) AND (L11
                OR L12 OR L13 OR L14)
L102          1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L61 AND (P21 OR P 21)


=> s l38,l60,l88,l90,l101,l102 not l15,l61

L112          1 (L38 OR L60 OR L88 OR L90 OR L101 OR L102) NOT (L15 OR L61)

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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 27 Apr 2006 (20060427/PD)
FILE LAST UPDATED: 27 Apr 2006 (20060427/ED)
HIGHEST GRANTED PATENT NUMBER: US7036150
HIGHEST APPLICATION PUBLICATION NUMBER: US2006090232
CA INDEXING IS CURRENT THROUGH 27 Apr 2006 (20060427/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 27 Apr 2006 (20060427/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2006


=> d que l100

L98          612 SEA FILE=USPATFULL ABB=ON  PLU=ON  (P21 OR P 21)/TI,IT,AB,CLM
L99         5951 SEA FILE=USPATFULL ABB=ON  PLU=ON  (WRINKL? OR PHOTOAG? OR
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L100          1 SEA FILE=USPATFULL ABB=ON  PLU=ON  L99 AND L98


=> s l100

L113          1 L99 AND L98
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L7        11170 SEA FILE=CAPLUS ABB=ON  PLU=ON  (WRINKL? OR SKIN WRINKL? OR
                WRINK? REDUC?)
L37        1259 SEA FILE=CAPLUS ABB=ON  PLU=ON  P21 (L) (PROTEIN KINAS? OR
                SIGNAL TRANSDUCT?)
L38           1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L37 AND L7


L7        11170 SEA FILE=CAPLUS ABB=ON  PLU=ON  (WRINKL? OR SKIN WRINKL? OR
                WRINK? REDUC?)
L56           8 SEA FILE=CAPLUS ABB=ON  PLU=ON  SKIN, DISEASE (L) AGING+OLD/CT

L57           0 SEA FILE=CAPLUS ABB=ON  PLU=ON  PHOTO AGING/CT
L58        5521 SEA FILE=CAPLUS ABB=ON  PLU=ON  (SKIN OR PHOTO) (L) (AGING OR
                AGEING)
L59         979 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L56 OR L57 OR L58) AND L7
L60           1 SEA FILE=CAPLUS ABB=ON  PLU=ON  L59 AND (P21 OR P 21)


L1          658 SEA FILE=CAPLUS ABB=ON  PLU=ON  P21-ACTIVATED KINASE/CT
L2            0 SEA FILE=CAPLUS ABB=ON  PLU=ON  PROTEINS (L) P21/CT
L3            0 SEA FILE=CAPLUS ABB=ON  PLU=ON  PROTEINS (L) SIGNALING+OLD/CT
L4       142893 SEA FILE=CAPLUS ABB=ON  PLU=ON  SIGNAL TRANSDUCTION/CT
L5        88152 SEA FILE=CAPLUS ABB=ON  PLU=ON  (P21 OR P(2A)21 OR P21 PROTEIN
                KINASE OR P21 SIGNAL TRANSDUCTION? OR P21?)
L7        11170 SEA FILE=CAPLUS ABB=ON  PLU=ON  (WRINKL? OR SKIN WRINKL? OR
                WRINK? REDUC?)
L8           25 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4 OR L5)
                AND L7
L87       46461 SEA FILE=CAPLUS ABB=ON  PLU=ON  SCREENING/CW
L88           0 SEA FILE=CAPLUS ABB=ON  PLU=ON  L87 AND L8


L1          658 SEA FILE=CAPLUS ABB=ON  PLU=ON  P21-ACTIVATED KINASE/CT
L2            0 SEA FILE=CAPLUS ABB=ON  PLU=ON  PROTEINS (L) P21/CT
L3            0 SEA FILE=CAPLUS ABB=ON  PLU=ON  PROTEINS (L) SIGNALING+OLD/CT
L4       142893 SEA FILE=CAPLUS ABB=ON  PLU=ON  SIGNAL TRANSDUCTION/CT
L5        88152 SEA FILE=CAPLUS ABB=ON  PLU=ON  (P21 OR P(2A)21 OR P21 PROTEIN
                KINASE OR P21 SIGNAL TRANSDUCTION? OR P21?)
L7        11170 SEA FILE=CAPLUS ABB=ON  PLU=ON  (WRINKL? OR SKIN WRINKL? OR
                WRINK? REDUC?)
L8           25 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4 OR L5)
                AND L7
L89      734780 SEA FILE=CAPLUS ABB=ON  PLU=ON  9/SC,SX
L90           0 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 AND L89


L1          658 SEA FILE=CAPLUS ABB=ON  PLU=ON  P21-ACTIVATED KINASE/CT
L2            0 SEA FILE=CAPLUS ABB=ON  PLU=ON  PROTEINS (L) P21/CT
L3            0 SEA FILE=CAPLUS ABB=ON  PLU=ON  PROTEINS (L) SIGNALING+OLD/CT
L4       142893 SEA FILE=CAPLUS ABB=ON  PLU=ON  SIGNAL TRANSDUCTION/CT
L5        88152 SEA FILE=CAPLUS ABB=ON  PLU=ON  (P21 OR P(2A)21 OR P21 PROTEIN
                KINASE OR P21 SIGNAL TRANSDUCTION? OR P21?)
L7        11170 SEA FILE=CAPLUS ABB=ON  PLU=ON  (WRINKL? OR SKIN WRINKL? OR
                WRINK? REDUC?)
L8           25 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4 OR L5)
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L110 1 L86 NOT L85

=> file biosis

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CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

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=> d que l76

L65 225 SEA FILE=BIOSIS ABB=ON PLU=ON P21 PROTEIN/CT
L66 3066 SEA FILE=BIOSIS ABB=ON PLU=ON P21/CT
L67 4 SEA FILE=BIOSIS ABB=ON PLU=ON SKIN AGING/CT
L68 2118 SEA FILE=BIOSIS ABB=ON PLU=ON (SKIN OR PHOTO) (L) (AGING OR AGEING)
L69 2403 SEA FILE=BIOSIS ABB=ON PLU=ON (WRINKL? OR SKIN WRINKL? OR WRINK? REDUC?)
L75 4 SEA FILE=BIOSIS ABB=ON PLU=ON (L65 OR L66) AND (L67 OR L68 OR L69)
L76 4 SEA FILE=BIOSIS ABB=ON PLU=ON L75 AND (P21 OR P 21)

=> s l76 not l74

L111 4 L76 NOT L74

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=> d que l38;d que l60; d que l88; d que l90; d que l101; d que l102

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=> d que l55

L20         2050 SEA FILE=MEDLINE ABB=ON  PLU=ON  RHO GTP-BINDING PROTEINS/CT
L21       171376 SEA FILE=MEDLINE ABB=ON  PLU=ON  SIGNAL TRANSDUCTION+NT/CT
L22         1597 SEA FILE=MEDLINE ABB=ON  PLU=ON  INTRACELLULAR SIGNALING
                 PEPTIDES AND PROTEINS/CT
L23        27550 SEA FILE=MEDLINE ABB=ON  PLU=ON  (P21 OR P(2A)21 OR P21
                 PROTEIN KINASE OR P21 SIGNAL TRANSDUCT?)
L51         2229 SEA FILE=MEDLINE ABB=ON  PLU=ON  SKIN AGING/CT
L52         4153 SEA FILE=MEDLINE ABB=ON  PLU=ON  (SKIN OR PHOTO) (L) (AGING OR
                 AGEING)
L53           64 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L51 OR L52) AND (L20 OR L21
                 OR L22 OR L23)
L54           12 SEA FILE=MEDLINE ABB=ON  PLU=ON  L53 AND (P21 OR P 21)
L55            5 SEA FILE=MEDLINE ABB=ON  PLU=ON  L54 NOT PY>2002


=> s l55 not l27

L109          5 L55 NOT L27

=> file wpix

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>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<



>>>  UPCOMING NEW DWPI: EFFECTS ON SCRIPT RUNS - SEE NEWS MESSAGE <<<
'BIX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

=> d que l86

L81           16 SEA FILE=WPIX ABB=ON  PLU=ON  P21/BIX (L) SIGNAL TRANSDUCT?/BIX

L82           39 SEA FILE=WPIX ABB=ON  PLU=ON  P21/BIX (L) PROTEIN KINAS?/BIX
L83          951 SEA FILE=WPIX ABB=ON  PLU=ON  (P21/BIX OR P 21/BIX)
L84        22202 SEA FILE=WPIX ABB=ON  PLU=ON  (WRINKL?/BIX OR SKIN WRINKL?/BIX
                 OR WRINK? REDUC?/BIX OR SKIN AGING/BIX OR SKIN AGEING/BIX OR
                 PHOTO/BIX (L) (AGING/BIX OR AGEING/BIX))
L86            2 SEA FILE=WPIX ABB=ON  PLU=ON  (L81 OR L82 OR L83) AND L84


=> s l86 not l85
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L108 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:240313 CAPLUS
DOCUMENT NUMBER: 112:240313
TITLE: Cosmetic skin preparations containing nicorandil
INVENTOR(S): Nakayama, Taiichi; **Fujii, Seishiro**; Kitamura, Kenji
PATENT ASSIGNEE(S): Shiseido Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 02032006	A2	19900201	JP 1988-180228	19880721
PRIORITY APPLN. INFO.:			JP 1988-180228	19880721

ED Entered STN: 23 Jun 1990
AB **Skin** prepns. contain N-(2-hydroxyethyl)nicotinamide nitrate ester (I) or its salts as an active ingredient. The prepns. prevent **aging** of the **skin** and damages caused by suntan, razors, etc. Glycerin 4.0, 1,3-butylene glycol 4.0, EtOH 7.0, poly(oxyethylene) oleyl ether 0.5, I 0.01, and H2O to 100% by weight to give a shaving lotion.
IC ICM A61K007-00
ICS A61K007-15; A61K031-44
CC 62-4 (Essential Oils and Cosmetics)
IT 65141-46-0, Nicorandil
RL: BIOL (Biological study)
(cosmetic **skin** prepns. containing, for prevention of **aging** and damaging)

=> □

=> file medline
FILE 'MEDLINE' ENTERED AT 16:51:32 ON 28 APR 2006

FILE LAST UPDATED: 27 APR 2006 (20060427/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

halo, lower alkoxy) or II (R2-3 = H, alkyl). I and II have strong retinoic acid-like effects and show reduced cytotoxicity due to rapid in vivo metabolism, and are useful for prevention of **skin** damages from sunlight and **aging**. I (R1 = H) (III), prepared from 3-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2-propenoic acid and 4-HOC6H4CO2H, enhanced EGF-dependent proliferation of fibroblast and also showed other **skin** damage-protecting effects. A cosmetic lotion containing III was formulated.

IC ICM A61K007-48
ICS A61K007-00; A61K031-215; C07C069-608

CC 62-4 (Essential Oils and Cosmetics)
Section cross-reference(s): 1, 63

IT **Aging**
Cosmetics
Skin, disease
Sunscreens
(**skin** prepns. containing retinoids for prevention of **skin** damage from sunburn and **aging**)

IT Retinoids
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**skin** prepns. containing retinoids for prevention of **skin** damage from sunburn and **aging**)

IT Pharmaceutical dosage forms
(topical, **skin** prepns. containing retinoids for prevention of **skin** damage from sunburn and **aging**)

IT 99-96-7, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification with cyclohexenylpropenoic acid derivative; **skin** prepns. containing retinoids for prevention of **skin** damage from sunburn and **aging**)

IT 4951-39-7, 3-(2,6,6-Trimethyl-1-cyclohexen-1-yl)-2-propenoic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification with hydroxybenozic acid; **skin** prepns. containing retinoids for prevention of **skin** damage from sunburn and **aging**)

IT 22824-31-3, 5,6,7,8-Tetrahydro-5,5,8,8-tetramethyl-2-naphthol
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification with muconic acid; **skin** prepns. containing retinoids for prevention of **skin** damage from sunburn and **aging**)

IT 505-70-4, 2,4-Hexadienedioic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification with tetrahydronaphthol derivative; **skin** prepns. containing retinoids for prevention of **skin** damage from sunburn and **aging**)

IT 153233-07-9P
RL: PNU (Preparation, unclassified); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(selective hydrolysis of; **skin** prepns. containing retinoids for prevention of **skin** damage from sunburn and **aging**)

IT 153233-08-0P 153233-09-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**skin** prepns. containing retinoids for prevention of **skin** damage from sunburn and **aging**)

synthase inhibitors to prevent and reduce wrinkles. L-NAME treated mice show a reduction in fine wrinkles compared to untreated control mice which can prevent the formation of wrinkles caused by UVB exposure.

IC ICM A61K007-00
ICS A61K007-42; A61K007-44; A61K031-495

CC 62-4 (Essential Oils and Cosmetics)
Section cross-reference(s): 63

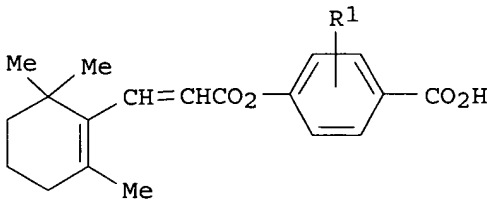
IT **Skin**, disease
(**aging**; NOS inhibitors for treatment of wrinkles)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

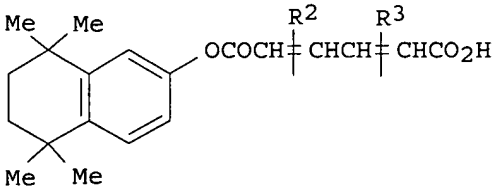
L108 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:677661 CAPLUS
DOCUMENT NUMBER: 123:92914
TITLE: Preparation of retinoids for preventing skin damages and skin preparations containing them
INVENTOR(S): Ehama, Ritsuko; Sakamoto, Okihiko; Horii, Izumi; Akima, Kazuo; **Fujii, Seishiro**; Shudo, Koichi
PATENT ASSIGNEE(S): Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07118134	A2	19950509	JP 1992-125625	19920417

PRIORITY APPLN. INFO.: JP 1992-125625 19920417
OTHER SOURCE(S): MARPAT 123:92914
ED Entered STN: 15 Jul 1995
GI



I



II

AB The **skin** prepns. contain retinoids I (R1 = H, lower alkyl, OH,

WO 2005123010 A1 20051229 WO 2005-US20666 20050610
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2004-578799P P 20040610
ED Entered STN: 15 Dec 2005
AB Disclosed is, inter alia, a method of reducing UVB-induced wrinkles in a subject, the method that includes: administering to a subject having, or at risk for, UVB-induced wrinkle, a composition comprising an agent that inhibits ATR mediated signaling. Thus, topical 1.2% caffeine in acetone was prepared and applied on the back of UVB irradiated and non-UVB irradiated mice. Caffeine was effective in reducing UVB-induced wrinkle formation.
IC ICM A61K007-42
ICS A61K031-522
INCL 424059000; 514263340
CC 62-4 (Essential Oils and Cosmetics)
IT **Skin**, disease
(**aging**, wrinkles, inhibition of; topical caffeine for inhibition of ATR mediated signaling for reducing UVB-induced wrinkles)

L108 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:615365 CAPLUS
DOCUMENT NUMBER: 137:159039
TITLE: NOS inhibitors for treatment of wrinkles
INVENTOR(S): **Fujii, Seishiro**; Lerner, Ethan
PATENT ASSIGNEE(S): The General Hospital Corporation, USA
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062306	A1	20020815	WO 2002-US2292	20020125
W: JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
US 2002168325	A1	20021114	US 2002-57247	20020125
EP 1359885	A1	20031112	EP 2002-720854	20020125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2004520388	T2	20040708	JP 2002-562314	20020125
US 2003207844	A1	20031106	US 2003-406306	20030403

PRIORITY APPLN. INFO.: US 2001-264176P P 20010125
US 2002-57247 A3 20020125
WO 2002-US2292 W 20020125
ED Entered STN: 16 Aug 2002
AB Methods, compns., and kits, are provided for the use of nitric oxide

Foundation of the University of Central Florida
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005077019	A2	20050825	WO 2005-US3908	20050207
WO 2005077019	A3	20060216		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005250799	A1	20051110	US 2005-52149	20050207

PRIORITY APPLN. INFO.: US 2004-542187P P 20040205
OTHER SOURCE(S): MARPAT 143:234993
ED Entered STN: 26 Aug 2005
AB Methods, compns., and kits are provided for the use of inhibitors of protease, i.e., caspase or serine protease involved in apoptosis to reduce wrinkles or other skin damage caused by exposure to UVB radiation. The protease inhibitor is administered, e.g., topically in a cosmetic or therapeutic composition Thus, UCF-101, an Omi/HtrA2 serine protease inhibitor was non-irritating to UVB-exposed skin in mice. Inhibition of Omi/HtrA2 serine protease by 1% UCF-101 in DMSO was effective at preventing and reducing UVB-induced wrinkle formation in mice. It was also effective at reducing UVB-induced dilation of blood vessels.
IC ICM A61K
CC 62-4 (Essential Oils and Cosmetics)
Section cross-reference(s): 1, 63
IT **Skin**, disease
(**aging**; topical compns. containing protease inhibitors for treatment of UVB-induced **skin** damage and wrinkles)

L108 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1308526 CAPLUS
DOCUMENT NUMBER: 144:40401
TITLE: Topical caffeine for inhibition of ATR mediated signaling for reducing UVB-induced wrinkles
INVENTOR(S): Nghiem, Paul; **Fujii, Seishiro**
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 13 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005276765	A1	20051215	US 2005-149126	20050609

D05-H09; D05-H12A; D05-H12D5; D05-H14B2; D05-H17A6; D05-H18; D09-E01
AN 2004-295301 [27] WPIX
AB WO2004026249 A UPAB: 20040426
NOVELTY - Screening of **wrinkles reducing** agent involves determination of the test agent to increase or induces a component (C1) of the **p21 signal transduction** pathway and correlating the ability of the test agent to increase expression, activity or levels of (C1) with the agent's ability to reduce the appearance or formation of **wrinkles.**

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(a) a cosmetic composition comprising an agent that increases or induces **p21**;

(b) providing a record involves determination of the test agent to increase or induces **p21**;

(c) generating the record that correlates the ability of the test agent; and

(d) a kit comprises a composition comprising an agent that increases or induces (C1); and instructions for using the composition.

ACTIVITY - Dermatological.

MECHANISM OF ACTION - None given.

USE - As a cosmetic for preventing or treating **wrinkles**, for reducing the appearance or formation of **wrinkles** on the skin (claimed) and in the manufacture of medicament for preventing skin damage e.g. UVB-induce skin damage.

ADVANTAGE - The **p21 signal transduction** pathway prevents skin damage, reduces the appearance or formation of **wrinkles** on the skin and UVB-induce skin damage.

Dwg.0/0

TECH UPTX: 20040426
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: The method further involving evaluating the effect of the agent on UVB-induced **wrinkles** on the skin of a subject and selecting the test agent that increases expression, activity or levels of (C1). Determination involves providing a cell, tissue or non-human subject comprising an exogenous nucleic acid comprising a regulatory region of (C1) operably linked to a nucleotide sequence encoding a reporter polypeptide and evaluating the ability of the test agent to increase the activity of the reporter polypeptide in the cell, tissue or non-human subject. The test agent is determined to increase or induce (C1) if it increases the activity of the reporter polypeptide.
Preferred Composition: The composition further comprises a cosmetic ingredient.
Preferred Components: The cosmetic ingredient is fragrance or sunscreen. The component of the **p21 signal transduction** pathway is **p21.**

TECHNOLOGY FOCUS - BIOLOGY - Preferred Components: The test agent is animal extract, botanical extract, fungal extract, small molecule, protein, lipid or nucleic acid.

L108 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:902724 CAPLUS
DOCUMENT NUMBER: 143:234993
TITLE: Protease inhibitors for treatment of wrinkles
INVENTOR(S): **Fujii, Seishiro**; Hirakawa, Satoshi; Detmar, Michael; Zervos, Antonis S.
PATENT ASSIGNEE(S): The General Hospital Corporation, USA; Research